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FILE 'HOME' ENTERED AT 13:16:25 ON 09 MAY 2007

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SINCE FILE

TOTAL

ENTRY

SESSION

FULL ESTIMATED COST

0.21

0.21

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2 37

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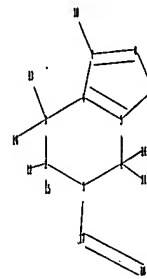
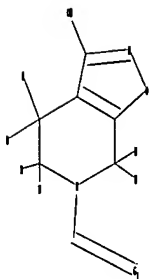
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NEWS 7 JAN 22 CA/CAPplus enhanced with patent applications from India
NEWS 8 JAN 29 PHAR reloaded with new search and display fields
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NEWS 11 FEB 15 RUSSIAPAT enhanced with pre-1994 records
NEWS 12 FEB 23 KOREAPAT enhanced with IPC 8 features and functionality
NEWS 13 FEB 26 MEDLINE reloaded with enhancements
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NEWS 15 FEB 26 TOXCENTER enhanced with reloaded MEDLINE
NEWS 16 FEB 26 IFICDB/IFIPAT/IFIUDB reloaded with enhancements
NEWS 17 FEB 26 CAS Registry Number crossover limit increased from 10,000 to 300,000 in multiple databases
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NEWS 19 MAR 16 CASREACT coverage extended
NEWS 20 MAR 20 MARPAT now updated daily
NEWS 21 MAR 22 LWPI reloaded
NEWS 22 MAR 30 RDISCLOSURE reloaded with enhancements
NEWS 23 APR 02 JICST-EPLUS removed from database clusters and STN
NEWS 24 APR 30 GENBANK reloaded and enhanced with Genome Project ID field
NEWS 25 APR 30 CHEMCATS enhanced with 1.2 million new records
NEWS 26 APR 30 CA/CAPplus enhanced with 1870-1889 U.S. patent records
NEWS 27 APR 30 INPADOC replaced by INPADOCDB on STN
NEWS 28 MAY 01 New CAS web site launched
NEWS 29 MAY 08 CA/CAPplus Indian patent publication number format defined

NEWS EXPRESS NOVEMBER 10 CURRENT WINDOWS VERSION IS V8.01c, CURRENT MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP), AND CURRENT DISCOVER FILE IS DATED 25 SEPTEMBER 2006.

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chain nodes :
 10 11 12 13 14 15 16 17 18
 ring nodes :
 1 2 3 4 5 6 7 8 9
 chain bonds :
 1-17 2-12 2-15 3-13 3-14 6-11 6-16 7-10 17-18
 ring bonds :
 1-2 1-6 2-3 3-4 4-5 4-7 5-6 5-9 7-8 8-9
 exact/norm bonds :
 1-2 1-6 1-17 2-3 3-4 4-5 4-7 5-6 5-9 7-8 7-10 8-9 17-18
 exact bonds :
 2-12 2-15 3-13 3-14 6-11 6-16

G1:O,S,N

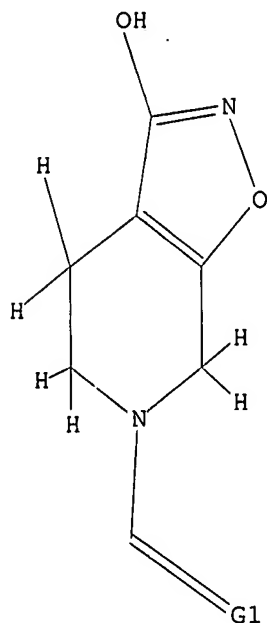
Match level :
 1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:CLASS
 11:CLASS 12:CLASS 13:CLASS 14:CLASS 15:CLASS 16:CLASS 17:CLASS 18:CLASS

L1 STRUCTURE UPLOADED

=> D L1

L1 HAS NO ANSWERS

L1 STR



G1 O,S,N

Structure attributes must be viewed using STN Express query preparation.

=> s l1

SAMPLE SEARCH INITIATED 13:17:20 FILE 'REGISTRY'

SAMPLE SCREEN SEARCH COMPLETED - 2 TO ITERATE

100.0% PROCESSED 2 ITERATIONS 0 ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE **COMPLETE**
BATCH **COMPLETE**
PROJECTED ITERATIONS: 2 TO 124
PROJECTED ANSWERS: 0 TO 0

L2 0 SEA SSS SAM L1

=> s l1 full

FULL SEARCH INITIATED 13:17:25 FILE 'REGISTRY'

FULL SCREEN SEARCH COMPLETED - 55 TO ITERATE

100.0% PROCESSED 55 ITERATIONS 3 ANSWERS
SEARCH TIME: 00.00.01

L3 3 SEA SSS FUL L1

=> file caplus

COST IN U.S. DOLLARS

| SINCE FILE | TOTAL |
|------------|---------|
| ENTRY | SESSION |
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FULL ESTIMATED COST

FILE 'CAPLUS' ENTERED AT 13:17:29 ON 09 MAY 2007
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FILE COVERS 1907 - 9 May 2007 VOL 146 ISS 20
FILE LAST UPDATED: 8 May 2007 (20070508/ED)

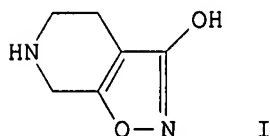
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L4 9 L3

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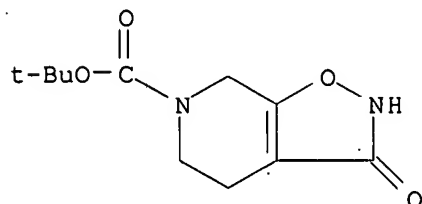
L4 ANSWER 1 OF 9 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1990:111431 CAPLUS
DOCUMENT NUMBER: 112:111431
TITLE: Enzymic synthesis of two glucuronides of the hydroxyisoxazole GABA-agonist, THIP, and the in vivo glucuronidation of THIP in rat
AUTHOR(S): Andersen, J. V.; Dalgaard, L.; Hansen, S. H.
CORPORATE SOURCE: PharmaBiote Res. Cent., R. Dan. Sch. Pharm., Copenhagen, DK-2100, Den.
SOURCE: Xenobiotica (1989), 19(12), 1399-1406
CODEN: XENOBH; ISSN: 0049-8254
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



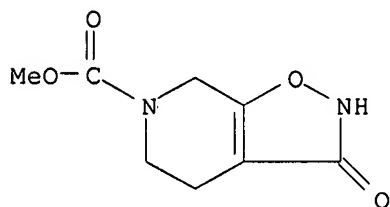
AB A method for the preparative enzymic synthesis of two glucuronides of THIP (3-hydroxy-4,5,6,7-tetrahydroisoxazolo[5,4-c]pyridine) (I) is described. Using FAB mass spectrometry, UV and 1H- and 13C-NMR spectroscopy, the two glucuronides were identified as N- and O-glucuronides. An HPLC method for determination of THIP and the two glucuronides in urine was developed. The glucuronidation pattern of THIP in rats was examined; THIP was excreted as THIP-O-glucuronide but not as THIP-N-glucuronide.

IT 83491-28-5P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and glucuronidation of)

RN 83491-28-5 CAPLUS
CN Isoxazolo[5,4-c]pyridine-6(2H)-carboxylic acid, 3,4,5,7-tetrahydro-3-oxo-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



L4 ANSWER 2 OF 9 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1985:6268 CAPLUS
DOCUMENT NUMBER: 102:6268
TITLE: Synthesis of 3-isoxazolols revisited. Diketene and β -oxo esters as starting materials
AUTHOR(S): Jacobsen, Niels; Kolind-Andersen, Hans; Christensen, Jens
CORPORATE SOURCE: Res. Dev. Dep., Cheminova Ltd., Lemvig, DK-7620, Den.
SOURCE: Canadian Journal of Chemistry (1984), 62(10), 1940-4
CODEN: CJCHAG; ISSN: 0008-4042
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 102:6268
AB 3-Isioxazolols were prepared in good yield by cyclocondensation of β -oxo esters or diketene with H_2NOH , by maintaining pH .apprx.10 throughout the reaction and quenching the reaction mixture with an excess of strong mineral acid. This suppresses the formation of 5-isioxazolones, which are otherwise normally the main product of the reaction.
IT 65202-62-2P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of, by hydroxylamine cyclocondensation with β -oxo ester)
RN 65202-62-2 CAPLUS
CN Isoxazolo[5,4-c]pyridine-6(2H)-carboxylic acid, 3,4,5,7-tetrahydro-3-oxo-, methyl ester (9CI) (CA INDEX NAME)



L4 ANSWER 3 OF 9 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1984:465548 CAPLUS
DOCUMENT NUMBER: 101:65548
TITLE: Analgesic GABA agonists. Synthesis and structure-activity studies on analogs and derivatives of muscimol and THIP
AUTHOR(S): Haeffliger, Walter; Revesz, Laszlo; Maurer, Richard; Roemer, Dietmar; Buescher, Heinz Hermann
CORPORATE SOURCE: Sandoz Ltd., Basel, CH-4002, Switz.
SOURCE: European Journal of Medicinal Chemistry (1984), 19(2), 149-56
CODEN: EJMCA5; ISSN: 0009-4374
DOCUMENT TYPE: Journal
LANGUAGE: English

OTHER SOURCE(S): CASREACT 101:65548

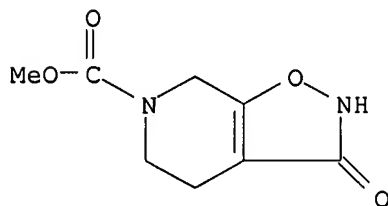
AB A series of analogs. and derivs. (prodrugs) of muscimol and THIP were prepared and their GABA receptor affinity, analgesic, and GABAergic properties examined. Some compds. designed as prodrugs exhibited high GABA receptor affinity indicating that nonzwitterionic mols. interact with GABA receptors. Analgesic and GABAergic activities of muscimol prodrugs were pronounced but weaker than muscimol itself. A ring opened THIP derivative was inactive whereas its carbamate derivative showed analgesic and GABAergic activity. A benzophenone-imine derivative showed strong GABA binding but no analgesic activity. Carbamate type THIP prodrugs were also active in analgesic and anticonvulsive tests but weaker than THIP itself. Ester- and alkanoyloxymethyl prodrugs were only active in the hot plate test. When the inactive 7-methyl-THIP was converted to a potential prodrug it produced high GABA-mimetic activity in both anticonvulsant and analgesic tests. In all cases, sedation was inseparable from analgesia.

IT 65202-62-2

RL: BIOL (Biological study)
(reaction with phenol sulfonyl chloride)

RN 65202-62-2 CAPLUS

CN Isoxazolo[5,4-c]pyridine-6(2H)-carboxylic acid, 3,4,5,7-tetrahydro-3-oxo-, methyl ester (9CI) (CA INDEX NAME)



L4 ANSWER 4 OF 9 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1982:582395 CAPLUS

DOCUMENT NUMBER: 97:182395

TITLE: 2-Acyl-4,5,6,7-tetrahydroisoxazolo[5,4-c]pyridin-3-ones, their use as medicines and their pharmaceutical compositions

INVENTOR(S): Perregaard, Jens Kristian

PATENT ASSIGNEE(S): Kefalas A/S, Den.

SOURCE: Fr. Demande, 18 pp.

CODEN: FRXXBL

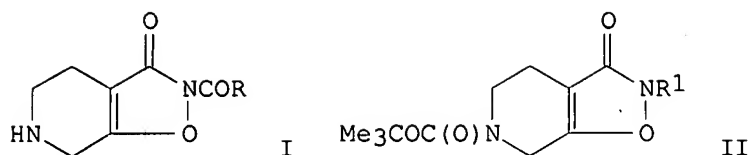
DOCUMENT TYPE: Patent

LANGUAGE: French

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
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| ----- | ---- | ----- | ----- | ----- |
| FR 2494691 | A1 | 19820528 | FR 1981-22328 | 19811127 |
| DE 3145473 | A1 | 19820826 | DE 1981-3145473 | 19811116 |
| GB 2088370 | A | 19820609 | GB 1981-34744 | 19811118 |
| GB 2088370 | B | 19840801 | | |
| DK 8105242 | A | 19820528 | DK 1981-5242 | 19811126 |
| JP 57118584 | A | 19820723 | JP 1981-189409 | 19811127 |
| PRIORITY APPLN. INFO.: | | | GB 1980-38140 | A 19801127 |
| OTHER SOURCE(S): | CASREACT 97:182395 | | | |
| GI | | | | |

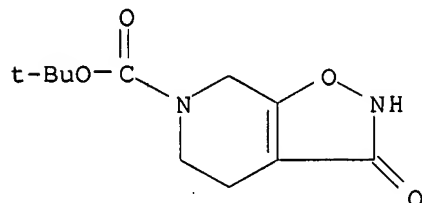


AB Title compds. I (R = alkyl, Ph, alkyl-, alkoxy-, or halophenyl, phenylalkyl, alkoxy, NH₂, NHPH, cyclohexylamino) were prepared, and they exhibited anticonvulsant activity (formulations are also given). II (R₁ = H) was heated with (PhCO)₂O, and the II (R₁ = CPh) obtained was treated with CF₃CO₂H to give I (R = Ph).

IT 83491-28-5P
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
 (preparation and N-acylation of)

RN 83491-28-5 CAPLUS

CN Isoxazolo[5,4-c]pyridine-6(2H)-carboxylic acid, 3,4,5,7-tetrahydro-3-oxo-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



L4 ANSWER 5 OF 9 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1982:582394 CAPLUS

DOCUMENT NUMBER: 97:182394

TITLE: 3-Substituted 4,5,6,7-tetrahydroisoxazolo[5,4-c]pyridines and their pharmaceutical compositions

INVENTOR(S): Perregaard, Jens Kristian

PATENT ASSIGNEE(S): Kefalas A/S, Den.

SOURCE: Fr. Demande, 18 pp.
 CODEN: FRXXBL

DOCUMENT TYPE: Patent

LANGUAGE: French

FAMILY ACC. NUM. COUNT: 1

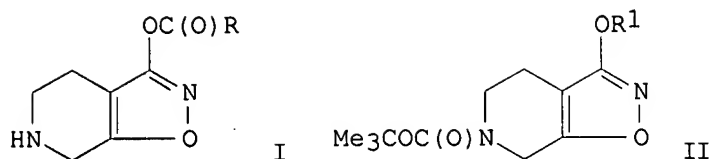
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
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| FR 2494692 | A1 | 19820528 | FR 1981-22329 | 19811127 |
| DE 3145474 | A1 | 19820902 | DE 1981-3145474 | 19811116 |
| GB 2088371 | A | 19820609 | GB 1981-34746 | 19811118 |
| GB 2088371 | B | 19840718 | | |
| DK 8105241 | A | 19820528 | DK 1981-5241 | 19811126 |
| JP 57118583 | A | 19820723 | JP 1981-189408 | 19811127 |
| US 4353910 | A | 19821012 | US 1981-325292 | 19811127 |
| | | | GB 1980-38139 | A 19801127 |

PRIORITY APPLN. INFO.: GB 1980-38139

OTHER SOURCE(S): CASREACT 97:182394; MARPAT 97:182394

GI



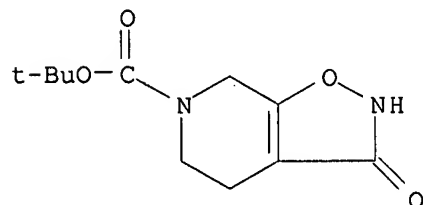
AB Title compds. I (R = alkyl, Ph, alkyl-, alkoxy-, or halophenyl, phenylalkyl, alkoxy, NH₂, substituted amino), which were prepared, showed anticonvulsant, muscle relaxant, and analgesic activity. II (R₁ = H) was treated with AcCl, and the II (R₁ = Ac) product was treated with CF₃CO₂H to give I (R = Me).

IT 83491-28-5P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and O-acylation of)

RN 83491-28-5 CAPLUS

CN Isoxazolo[5,4-c]pyridine-6(2H)-carboxylic acid, 3,4,5,7-tetrahydro-3-oxo-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



L4 ANSWER 6 OF 9 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1982:562964 CAPLUS

DOCUMENT NUMBER: 97:162964

TITLE: Isoxazolo[5,4-c]pyridines which are GABA-agonists

INVENTOR(S): Krogsgaard-Larsen, Povl

PATENT ASSIGNEE(S): Lundbeck, H., og Co. A/S, Den.

SOURCE: Can., 29 pp. Division of Can. Appl. No. 305,798..

CODEN: CAXXA4

DOCUMENT TYPE: Patent

LANGUAGE: English

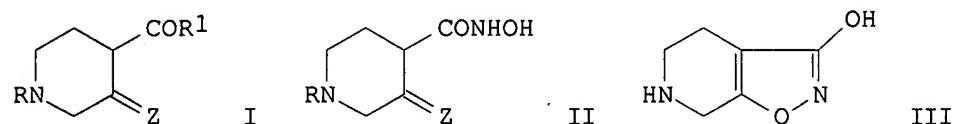
FAMILY ACC. NUM. COUNT: 3

PATENT INFORMATION:

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| CA 1125288 | A2 | 19820608 | CA 1981-377128 | 19810507 |
| CA 1107736 | A1 | 19810825 | CA 1978-305798 | 19780620 |
| US 4301287 | A | 19811117 | US 1979-104080 | 19791217 |
| PRIORITY APPLN. INFO.: | | | GB 1977-25740 | A 19770620 |
| | | | CA 1978-305798 | A3 19780620 |
| | | | US 1978-917118 | A3 19780619 |

OTHER SOURCE(S): MARPAT 97:162964

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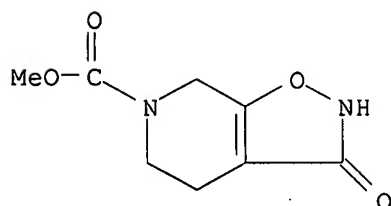


AB Piperidinecarboxylic acid compds. I (R = Ac, carbalkoxy, carbophenoxy, CPh₃, CHO; Z = ketalized O; R₁ = halo, OH, alkoxy) reacted with HONH₂ to yield hydroxamic acids II. Isoxazolo[5,4-c]pyridine derivative III, which is an agonist of H₂N(CH₂)₃CO₂H, was prepared from II. I (R = CO₂Me, R₁ = OEt, Z = OCH₂CH₂O) reacted with HONH₂ to give II (R = CO₂Me, Z = OCH₂CH₂O), and the latter was treated with HCl and then with HBr-HOAc to give III.HBr.

IT 65202-62-2P
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
 (preparation and hydrolysis-decarboxylation of)

RN 65202-62-2 CAPLUS

CN Isoxazolo[5,4-c]pyridine-6(2H)-carboxylic acid, 3,4,5,7-tetrahydro-3-oxo-, methyl ester (9CI) (CA INDEX NAME)



L4 ANSWER 7 OF 9 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1982:527546 CAPLUS

DOCUMENT NUMBER: 97:127546

TITLE: Deuterium labeling of the GABA agonists THIP, piperidine-4-sulfonic acid, and the GABA uptake inhibitor THPO

AUTHOR(S): Krogsgaard-Larsen, Povl; Johansen, Joergen Stage; Falch, Erik

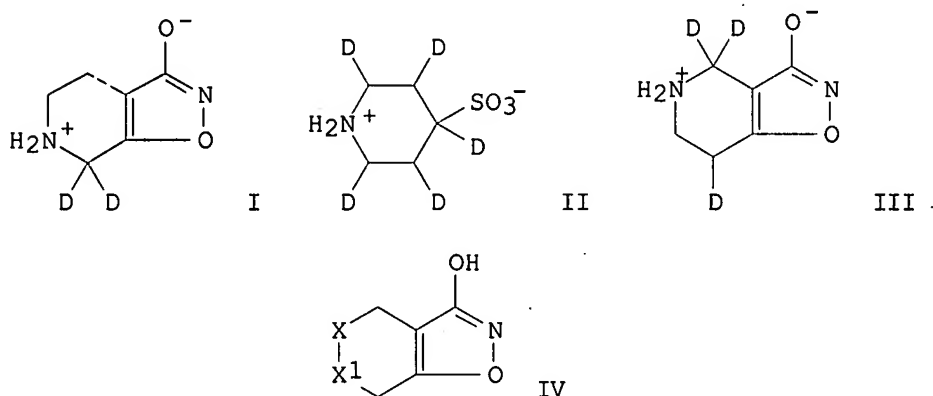
CORPORATE SOURCE: Dep. Chem. BC, R. Dan. Sch. Pharm., Copenhagen, DK-2100, Den.

SOURCE: Journal of Labelled Compounds and Radiopharmaceuticals (1982), 19(5), 689-702
 CODEN: JLCRD4; ISSN: 0362-4803

DOCUMENT TYPE: Journal

LANGUAGE: English

GI



AB The D-labeled title compds. (I, II, and III, resp.) were prepared I and III were prepared from IV (X = CH₂, X₁ = NCO₂Me; X = NCO₂Me, X₁ = CH₂), resp., by sequential methylation, N-decarboxylation, nitrosation, H-D

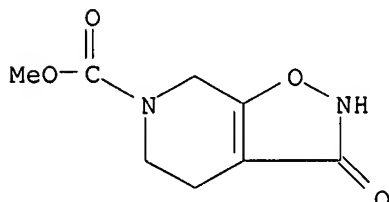
exchange reaction with D2O (acid- and base-catalyzed, resp.), denitrosation, and demethylation. Pt-catalyzed deuteration of pyridine-4-sulfonic acid in D2O gave II.

IT 65202-62-2

RL: RCT (Reactant); RACT (Reactant or reagent)
(methylation of)

RN 65202-62-2 CAPLUS

CN Isoxazolo[5,4-c]pyridine-6(2H)-carboxylic acid, 3,4,5,7-tetrahydro-3-oxo-, methyl ester (9CI) (CA INDEX NAME)



L4 ANSWER 8 OF 9 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1979:439458 CAPLUS

DOCUMENT NUMBER: 91:39458

TITLE: Methyl tetrahydrohydroxy isoxazolopyridine carboxylate

INVENTOR(S): Krogsgaard-Larsen, Povl

PATENT ASSIGNEE(S): Den.

SOURCE: Jpn. Kokai Tokkyo Koho, 13 pp.

CODEN: JKXXAF

DOCUMENT TYPE: Patent

LANGUAGE: Japanese

FAMILY ACC. NUM. COUNT: 3

PATENT INFORMATION:

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|-----------------------------------|------|----------|-----------------|----------|
| JP 54036290 | A | 19790316 | JP 1978-74800 | 19780620 |
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| DK 7802703 | A | 19781221 | DK 1978-2703 | 19780615 |
| FI 7801954 | A | 19781221 | FI 1978-1954 | 19780619 |
| FI 64376 | B | 19830729 | | |
| FI 64376 | C | 19831110 | | |
| FI 7801955 | A | 19781221 | FI 1978-1955 | 19780619 |
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| NO 152049 | B | 19850415 | | |
| NO 152449 | C | 19850724 | | |
| NO 7802128 | A | 19781221 | NO 1978-2128 | 19780619 |
| EP 167 | A1 | 19790110 | EP 1978-100190 | 19780619 |
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| EP 338 | A2 | 19790124 | EP 1978-100191 | 19780619 |
| EP 338 | A3 | 19790627 | | |
| EP 338 | B1 | 19811125 | | |
| R: BE, CH, DE, FR, GB, LU, NL, SE | | | | |
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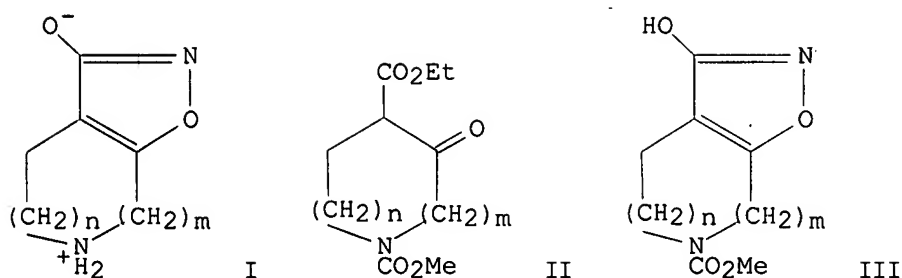
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GI

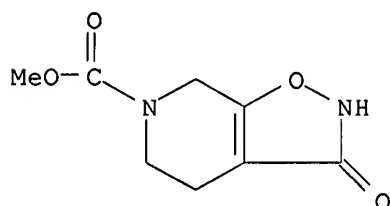


AB The 3-isoxazolol zwitterions 4,5,6,7-tetrahydroisoxazolo[5,4-c]pyridin-3-ol, (I, n = 1, m = 1), 5,6,7,8-tetrahydro-4H-isoxazolo[5,4-c]azepin-3-ol (I, n = 2, m = 1), and 5,6,7,8-tetrahydro-4H-isoxazolo[4,5-c]azepin-3-ol (I, n = 0, m = 3) were prepared. The starting materials were the cyclic β -oxoesters II. The ethylene acetals of II were treated with HONH₂ followed by deacetalization and cyclization of the intermediate β -oxohydroxamic acid ethylene acetals to give the resp. 3-isoxazolol derivs. III, which were transformed into the zwitterions I. The pK_A values of I were determined.

IT 65202-62-2P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and reaction with hydrogen bromide)

RN 65202-62-2 CAPLUS

CN Isoxazolo[5,4-c]pyridine-6(2H)-carboxylic acid, 3,4,5,7-tetrahydro-3-oxo-, methyl ester (9CI) (CA INDEX NAME)



=> d his

(FILE 'HOME' ENTERED AT 13:16:25 ON 09 MAY 2007)

FILE 'REGISTRY' ENTERED AT 13:16:33 ON 09 MAY 2007

L1 STRUCTURE UPLOADED
L2 0 S L1
L3 3 S L1 FULL

FILE 'CAPLUS' ENTERED AT 13:17:29 ON 09 MAY 2007

L4 9 S L3 FULL

=> log y

| | | |
|--|------------------|---------------|
| COST IN U.S. DOLLARS | SINCE FILE ENTRY | TOTAL SESSION |
| FULL ESTIMATED COST | 48.84 | 221.60 |
| DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS) | SINCE FILE ENTRY | TOTAL SESSION |
| CA SUBSCRIBER PRICE | -7.02 | -7.02 |

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NEWS 24 APR 30 GENBANK reloaded and enhanced with Genome Project ID field
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NEWS EXPRESS NOVEMBER 10 CURRENT WINDOWS VERSION IS V8.01c, CURRENT MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP), AND CURRENT DISCOVER FILE IS DATED 25 SEPTEMBER 2006.

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=> FILE CASREACT

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TOTAL

ENTRY

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FULL ESTIMATED COST

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0.21

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FILE CONTENT:1840 - 5 May 2007 VOL 146 ISS 20

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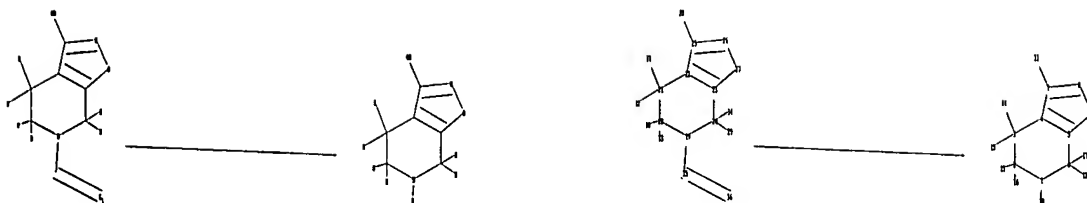
*
* CASREACT now has more than 12 million reactions *
*

Some CASREACT records are derived from the ZIC/VINITI database (1974-1999) provided by InfoChem, INPI data prior to 1986, and Biotransformations database compiled under the direction of Professor Dr. Klaus Kieslich.

This file contains CAS Registry Numbers for easy and accurate substance identification.

=>

Uploading C:\Program Files\Stnexp\Queries\10570551b.str



chain nodes :
 11 12 13 14 15 16 17 18 28 29 30 31 32 33 34 35 36
 ring nodes :
 1 2 3 4 5 6 7 8 9 19 20 21 22 23 24 25 26 27
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 24-29 24-34 25-28 35-36
 ring bonds :
 1-2 1-6 2-3 3-4 4-5 4-7 5-6 5-9 7-8 8-9 19-20 19-24 20-21 21-22 22-23
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 exact/norm bonds :
 1-2 1-6 2-3 3-4 4-5 5-6 7-8 7-11 19-20 19-24 19-35 20-21 21-22 22-23
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 exact bonds :
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 isolated ring systems :
 containing 1 : 19 :

G1:O,S

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 12:CLASS 13:CLASS 14:CLASS 15:CLASS 16:CLASS 17:CLASS 18:CLASS 19:Atom
 20:Atom 21:Atom 22:Atom 23:Atom 24:Atom 25:Atom 26:Atom 27:Atom 28:CLASS
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 containing 1
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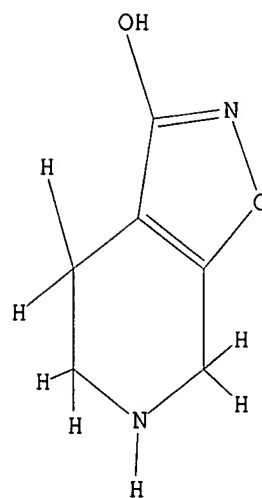
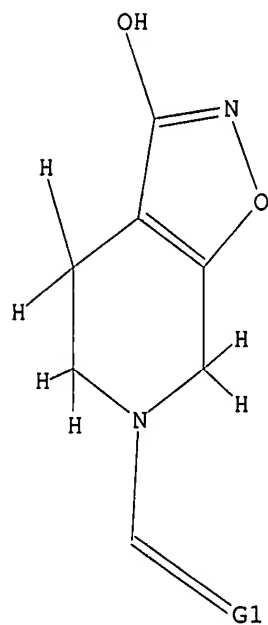
containing 19

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=> D L1

L1 HAS NO ANSWERS

L1 STR



G1 O,S

Structure attributes must be viewed using STN Express query preparation.

=> s l1 full

FULL SEARCH INITIATED 09:03:31 FILE 'CASREACT'

SCREENING COMPLETE - 22 REACTIONS TO VERIFY FROM

9 DOCUMENTS

100.0% DONE 22 VERIFIED

2 HIT RXNS

1 DOCS

SEARCH TIME: 00.00.01

L2 1 SEA SSS FUL L1 (2 REACTIONS)

=> d ibib abs fhit

L2 ANSWER 1 OF 1 CASREACT COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 88:37672 CASREACT

TITLE: Muscimol analogs. II. Synthesis of some bicyclic 3-isoxazolol zwitterions

AUTHOR(S): Krogsgaard-Larsen, Povl

CORPORATE SOURCE: Dep. Chem. BC, R. Dan. Sch. Pharm., Copenhagen, Den.

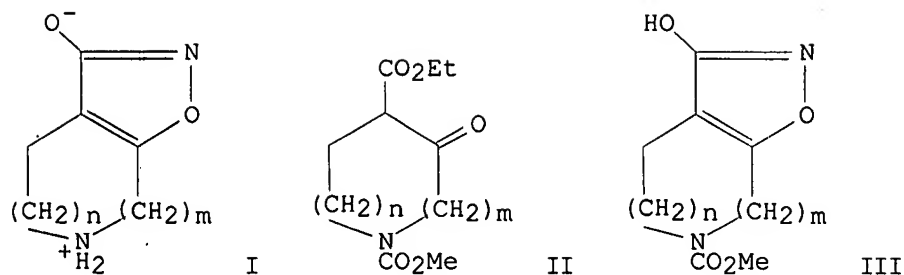
SOURCE: Acta Chemica Scandinavica, Series B: Organic Chemistry and Biochemistry (1977), B31(7), 584-8

CODEN: ACBOCV; ISSN: 0302-4369

DOCUMENT TYPE: Journal

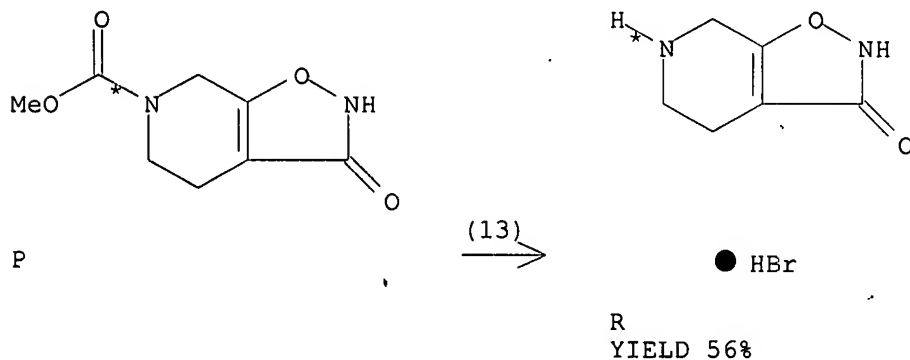
LANGUAGE: English

GI



AB The 3-isoxazolol zwitterions 4,5,6,7-tetrahydroisoxazolo[5,4-c]pyridin-3-ol, (I, n = 1, m = 1), 5,6,7,8-tetrahydro-4H-isoxazolo[5,4-c]azepin-3-ol (I, n = 2, m = 1), and 5,6,7,8-tetrahydro-4H-isoxazolo[4,5-c]azepin-3-ol (I, n = 0, m = 3) were prepared. The starting materials were the cyclic β -oxoesters II. The ethylene acetals of II were treated with HONH₂ followed by deacetalization and cyclization of the intermediate β -oxohydroxamic acid ethylene acetals to give the resp. 3-isoxazolol derivs. III, which were transformed into the zwitterions I. The pK_A values of I were determined

RX(13) OF 48 ...P ==> R...



RX(13) RCT P 65202-62-2
 RGT F 10035-10-6 HBr
 PRO R 65202-63-3

=> FIL STNGUIDE
 COST IN U.S. DOLLARS

FULL ESTIMATED COST

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)

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|------------------|---------------|
| 118.92 | 119.13 |
| -0.73 | -0.73 |

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FILE 'CASREACT' ENTERED AT 09:02:50 ON 09 MAY 2007
L1 . STRUCTURE UPLOADED
L2 1 S L1 FULL

FILE 'STNGUIDE' ENTERED AT 09:03:58 ON 09 MAY 2007

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SINCE FILE

. TOTAL

ENTRY

SESSION

FULL ESTIMATED COST

0.06

119.19

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0.21

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STRUCTURE FILE UPDATES: 8 MAY 2007 HIGHEST RN 934461-15-1

DICTIONARY FILE UPDATES: 8 MAY 2007 HIGHEST RN 934461-15-1

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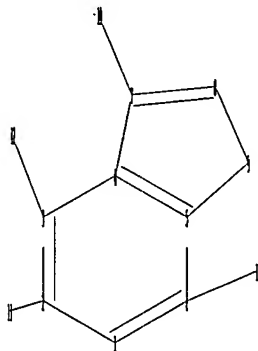
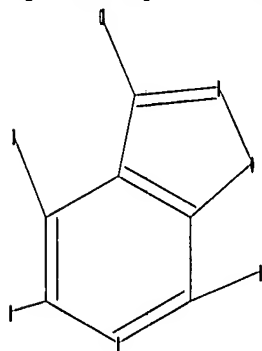
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ring nodes :

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chain bonds :

2-11 3-12 6-13 7-10

ring bonds :

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exact/norm bonds :

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exact bonds :

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normalized bonds :

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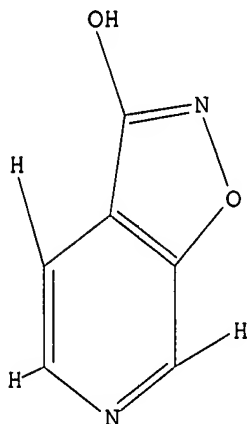
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:CLASS
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L1 STRUCTURE UPLOADED

=> d l1

L1 HAS NO ANSWERS

L1 STR



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SAMPLE SEARCH INITIATED 13:08:10 FILE 'REGISTRY'

SAMPLE SCREEN SEARCH COMPLETED - 1 TO ITERATE

100.0% PROCESSED 1 ITERATIONS

0 ANSWERS

SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE **COMPLETE**
BATCH **COMPLETE**

PROJECTED ITERATIONS: 1 TO 80

PROJECTED ANSWERS: 0 TO 0

L2 0 SEA SSS SAM L1

=> s l1 full

FULL SEARCH INITIATED 13:08:14 FILE 'REGISTRY'

FULL SCREEN SEARCH COMPLETED - 26 TO ITERATE

100.0% PROCESSED 26 ITERATIONS

3 ANSWERS

SEARCH TIME: 00.00.01

L3 3 SEA SSS FUL L1

=> file caplus

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172.55

172.76

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FILE LAST UPDATED: 8 May 2007 (20070508/ED)

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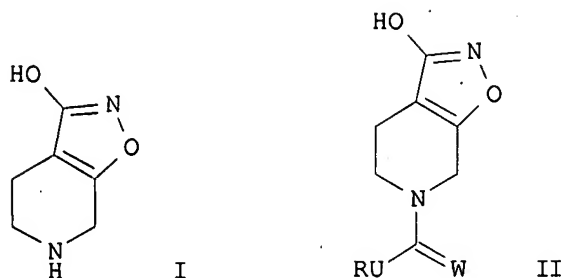
=> d ibib abs hitstr tot

L4 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:238996 CAPLUS
DOCUMENT NUMBER: 142:316828
TITLE: Method for the manufacture of THIP
INVENTOR(S): Petersen, Hans; Bech Sommer, Michael; Dancer, Robert
PATENT ASSIGNEE(S): H. Lundbeck A/S, Den.
SOURCE: PCT Int. Appl., 34 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------|----------|------------------|------------|
| WO 2005023820 | A1 | 20050317 | WO 2004-DK579 | 20040901 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | | |
| RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
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| EP 1664060 | A1 | 20060607 | EP 2004-762799 | 20040901 |
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| NO 2006001424 | A | 20060329 | NO 2006-1424 | 20060329 |
| PRIORITY APPLN. INFO.: | | | DK 2003-1277 | A 20030905 |
| | | | US 2003-500422P | P 20030905 |
| | | | WO 2004-DK579 | W 20040901 |

OTHER SOURCE(S):
GI

CASREACT 142:316828; MARPAT 142:316828



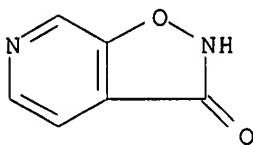
AB The present invention relates to a new method of preparing gaboxadol (THIP; I), which is useful for treating sleep disorders (no data). In particular a method of preparing THIP comprising reacting a compound II [R = alkyl, cycloalkyl, aryl, etc.; U = N, CR₁ (R₁ = H, R); W = O, S, NR₄ (R₄ = H, R)] or a salt thereof with an acid, typically a mineral acid, to obtain THIP as an acid addition salt. The present invention also relates to several intermediates. E.g., a multi-step synthesis of I.HBr, starting from Me 3-hydroxyisonicotinate, was given.

IT 847996-42-3P, Isoxazolo[5,4-c]pyridin-3(2H)-one
847996-43-4P

RL: IMF (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(method for the manufacture of THIP)

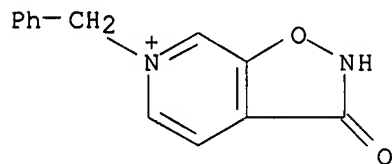
RN 847996-42-3 CAPLUS

CN Isoxazolo[5,4-c]pyridin-3(2H)-one (9CI) (CA INDEX NAME)



RN 847996-43-4 CAPLUS

CN Isoxazolo[5,4-c]pyridinium, 2,3-dihydro-3-oxo-6-(phenylmethyl)-, bromide
(9CI) (CA INDEX NAME)



● Br⁻

REFERENCE COUNT:

3

THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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COST IN U.S. DOLLARS

SINCE FILE

TOTAL

ENTRY

SESSION

FULL ESTIMATED COST

5.74

178.50

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)

SINCE FILE

TOTAL

ENTRY

SESSION

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-0.78

-0.78

STN INTERNATIONAL LOGOFF AT 13:08:42 ON 09 MAY 2007

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NEWS 19 MAR 16 CASREACT coverage extended
NEWS 20 MAR 20 MARPAT now updated daily
NEWS 21 MAR 22 LWPI reloaded
NEWS 22 MAR 30 RDISCLOSURE reloaded with enhancements
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NEWS 24 APR 30 GENBANK reloaded and enhanced with Genome Project ID field
NEWS 25 APR 30 CHEMCATS enhanced with 1.2 million new records
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NEWS EXPRESS NOVEMBER 10 CURRENT WINDOWS VERSION IS V8.01c, CURRENT MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP), AND CURRENT DISCOVER FILE IS DATED 25 SEPTEMBER 2006.

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FILE 'HOME' ENTERED AT 13:02:27 ON 09 MAY 2007

=> file reg

COST IN U.S. DOLLARS

SINCE FILE

TOTAL

ENTRY

SESSION

FULL ESTIMATED COST

0.21

0.21

FILE 'REGISTRY' ENTERED AT 13:02:36 ON 09 MAY 2007

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DICTIONARY FILE UPDATES: 8 MAY 2007 HIGHEST RN 934461-15-1

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TSCA INFORMATION NOW CURRENT THROUGH December 2, 2006

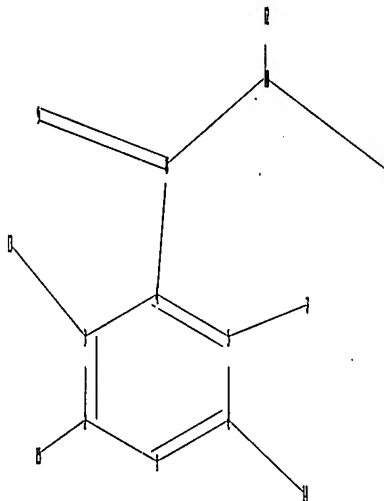
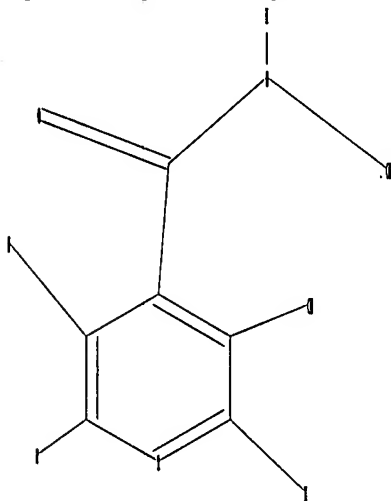
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<http://www.cas.org/support/stngen/stndoc/properties.html>

=>

Uploading C:\Program Files\Stnexp\Queries\10570551e.str



chain nodes :

7 8 9 10 11 12 13 14 15

ring nodes :

1 2 3 4 5 6

chain bonds :

2-15 3-13 4-8 5-7 6-14 8-9 8-10 10-11 10-12

ring bonds :

1-2 1-6 2-3 3-4 4-5 5-6

exact/norm bonds :

5-7 8-9 8-10 10-11

exact bonds :
 2-15 3-13 4-8 6-14 10-12
 normalized bonds :
 1-2 1-6 2-3 3-4 4-5 5-6
 isolated ring systems :
 containing 1 :

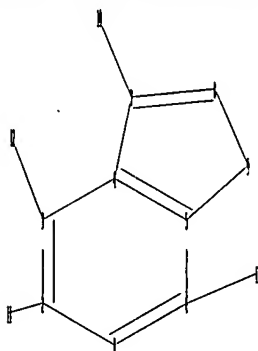
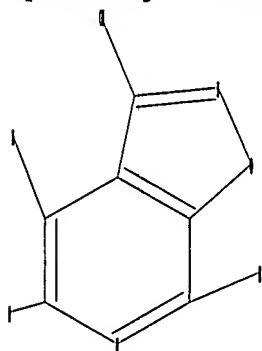
Match level :

1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:CLASS 8:CLASS 9:CLASS 10:CLASS
 11:CLASS 12:CLASS 13:CLASS 14:CLASS 15:CLASS

L1 STRUCTURE UPLOADED

=>

Uploading C:\Program Files\Stnexp\Queries\10570551d.str



chain nodes :
 10 11 12 13
 ring nodes :
 1 2 3 4 5 6 7 8 9
 chain bonds :
 2-11 3-12 6-13 7-10
 ring bonds :
 1-2 1-6 2-3 3-4 4-5 4-7 5-6 5-9 7-8 8-9
 exact/norm bonds :
 4-7 5-9 7-8 7-10 8-9
 exact bonds :
 2-11 3-12 6-13
 normalized bonds :
 1-2 1-6 2-3 3-4 4-5 5-6

Match level :

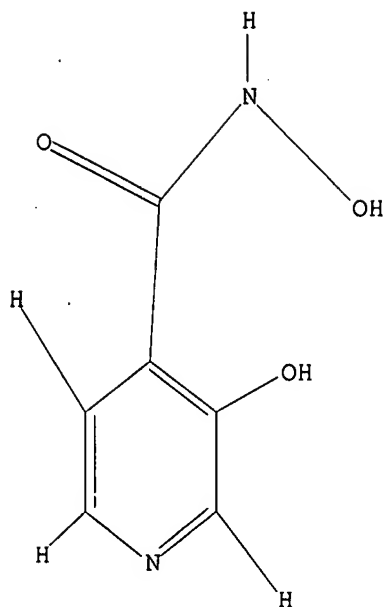
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:CLASS
 11:CLASS 12:CLASS 13:CLASS

L2 STRUCTURE UPLOADED

=> d 11

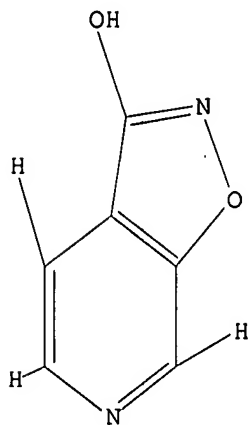
L1 HAS NO ANSWERS

L1 STR



Structure attributes must be viewed using STN Express query preparation.

```
=> d 12
L2 HAS NO ANSWERS
L2          STR
```



Structure attributes must be viewed using STN Express query preparation.

```
=> s 11 full
FULL SEARCH INITIATED 13:03:49 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED -      277 TO ITERATE

100.0% PROCESSED      277 ITERATIONS      1 ANSWERS
SEARCH TIME: 00.00.01
```

```
L3          1 SEA SSS FUL L1
```

```
=> s 12 full
FULL SEARCH INITIATED 13:04:04 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED -      26 TO ITERATE
```

100.0% PROCESSED 26 ITERATIONS
SEARCH TIME: 00.00.01

3 ANSWERS

L4 3 SEA SSS FUL L2

=> s 13 and 14 full
L5 0 L3 AND L4

=> log y

COST IN U.S. DOLLARS

SINCE FILE

TOTAL

ENTRY

SESSION

FULL ESTIMATED COST

344.65

344.86

STN INTERNATIONAL LOGOFF AT 13:04:16 ON 09 MAY 2007

Connecting via Winsock to STN

21

Welcome to STN International! Enter x:x

LOGINID:SSPTANXR1625

PASSWORD:

TERMINAL (ENTER 1, 2, 3, OR ?):2

* * * * * Welcome to STN International * * * * *

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NEWS 3 JAN 16 CA/CAPplus Company Name Thesaurus enhanced and reloaded
NEWS 4 JAN 16 IPC version 2007.01 thesaurus available on STN
NEWS 5 JAN 16 WPIDS/WPINDEXT/WPIX enhanced with IPC 8 reclassification data
NEWS 6 JAN 22 CA/CAPplus updated with revised CAS roles
NEWS 7 JAN 22 CA/CAPplus enhanced with patent applications from India
NEWS 8 JAN 29 PHAR reloaded with new search and display fields
NEWS 9 JAN 29 CAS Registry Number crossover limit increased to 300,000 in
multiple databases
NEWS 10 FEB 15 PATDPASPC enhanced with Drug Approval numbers
NEWS 11 FEB 15 RUSSIAPAT enhanced with pre-1994 records
NEWS 12 FEB 23 KOREAPAT enhanced with IPC 8 features and functionality
NEWS 13 FEB 26 MEDLINE reloaded with enhancements
NEWS 14 FEB 26 EMBASE enhanced with Clinical Trial Number field
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NEWS 25 APR 30 CHEMCATS enhanced with 1.2 million new records
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MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP),
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* * * * * STN Columbus * * * * *

FILE 'HOME' ENTERED AT 12:52:51 ON 09 MAY 2007

=> file reg

COST IN U.S. DOLLARS

SINCE FILE

TOTAL

ENTRY

SESSION

FULL ESTIMATED COST

0.21

0.21

FILE 'REGISTRY' ENTERED AT 12:53:03 ON 09 MAY 2007

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DICTIONARY FILE UPDATES: 8 MAY 2007 HIGHEST RN 934461-15-1

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TSCA INFORMATION NOW CURRENT THROUGH December 2, 2006

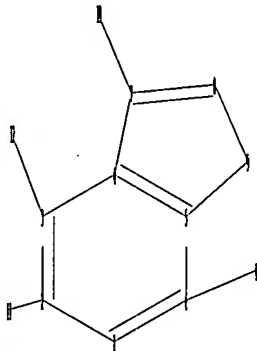
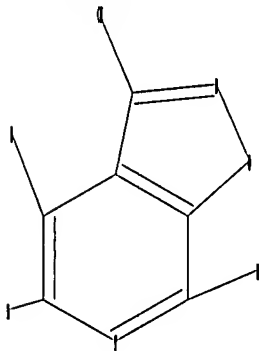
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REGISTRY includes numerically searchable data for experimental and predicted properties as well as tags indicating availability of experimental property data in the original document. For information on property searching in REGISTRY, refer to:

<http://www.cas.org/support/stngen/stndoc/properties.html>

=>

Uploading C:\Program Files\Stnexp\Queries\10570551d.str



chain nodes :

10 11 12 13

ring nodes :

1 2 3 4 5 6 7 8 9

chain bonds :

2-11 3-12 6-13 7-10

ring bonds :

1-2 1-6 2-3 3-4 4-5 4-7 5-6 5-9 7-8 8-9

exact/norm bonds :

4-7 5-9 7-8 7-10 8-9

exact bonds :

2-11 3-12 6-13

normalized bonds :

1-2 1-6 2-3 3-4 4-5 5-6

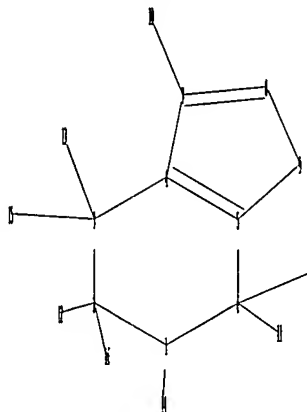
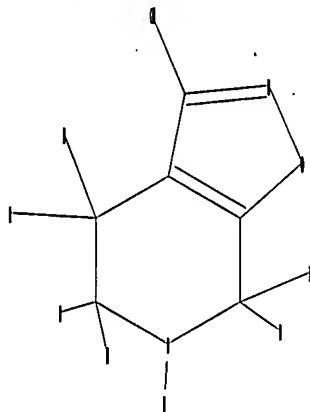
Match level :

1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:CLASS
11:CLASS 12:CLASS 13:CLASS

L1 STRUCTURE UPLOADED

=>

Uploading C:\Program Files\Stnexp\Queries\10570551C.str



chain nodes :

10 11 12 13 14 15 16 17

ring nodes :

1 2 3 4 5 6 7 8 9

chain bonds :

1-14 2-12 2-16 3-13 3-15 6-11 6-17 7-10

ring bonds :

1-2 1-6 2-3 3-4 4-5 4-7 5-6 5-9 7-8 8-9

exact/norm bonds :

1-2 1-6 2-3 3-4 4-5 4-7 5-6 5-9 7-8 7-10 8-9

exact bonds :

1-14 2-12 2-16 3-13 3-15 6-11 6-17

Match level :

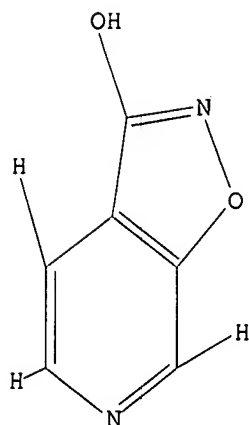
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:CLASS
11:CLASS 12:CLASS 13:CLASS 14:CLASS 15:CLASS 16:CLASS 17:CLASS

L2 STRUCTURE UPLOADED

=> d 11

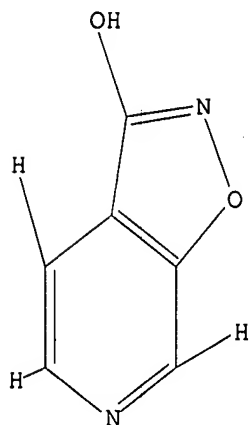
L1 HAS NO ANSWERS

L1 STR



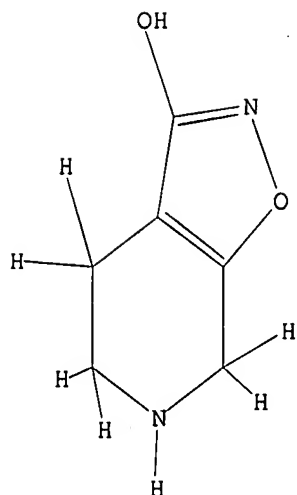
Structure attributes must be viewed using STN Express query preparation.

=> d 11
 L1 HAS NO ANSWERS
 L1 STR



Structure attributes must be viewed using STN Express query preparation.

=> d 12
 L2 HAS NO ANSWERS
 L2 STR



Structure attributes must be viewed using STN Express query preparation.

=> s 11 full

FULL SEARCH INITIATED 12:54:07 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED - 26 TO ITERATE

100.0% PROCESSED 26 ITERATIONS
SEARCH TIME: 00.00.01

3 ANSWERS

L3 3 SEA SSS FUL L1

=> s 12 ful

FULL SEARCH INITIATED 12:54:11 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED - 261 TO ITERATE

100.0% PROCESSED 261 ITERATIONS
SEARCH TIME: 00.00.01

36 ANSWERS

L4 36 SEA SSS FUL L2

=> s 13 and 14

L5 0 L3 AND L4

=> log y

COST IN U.S. DOLLARS

SINCE FILE

TOTAL

ENTRY

SESSION

FULL ESTIMATED COST

344.20

344.41

STN INTERNATIONAL LOGOFF AT 12:54:28 ON 09 MAY 2007

Q. 1

Connecting via Winsock to STN

Welcome to STN International! Enter x:x

LOGINID:SSPTANXR1625

PASSWORD:

TERMINAL (ENTER 1, 2, 3, OR ?):2

* * * * * Welcome to STN International * * * * *

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NEWS 3 JAN 16 CA/CAPplus Company Name Thesaurus enhanced and reloaded
NEWS 4 JAN 16 IPC version 2007.01 thesaurus available on STN
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NEWS 6 JAN 22 CA/CAPplus updated with revised CAS roles
NEWS 7 JAN 22 CA/CAPplus enhanced with patent applications from India
NEWS 8 JAN 29 PHAR reloaded with new search and display fields
NEWS 9 JAN 29 CAS Registry Number crossover limit increased to 300,000 in multiple databases
NEWS 10 FEB 15 PATDPASPC enhanced with Drug Approval numbers
NEWS 11 FEB 15 RUSSIAPAT enhanced with pre-1994 records
NEWS 12 FEB 23 KOREAPAT enhanced with IPC 8 features and functionality
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FILE 'HOME' ENTERED AT 12:37:09 ON 09 MAY 2007

=>

Uploading

THIS COMMAND NOT AVAILABLE IN THE CURRENT FILE

Do you want to switch to the Registry File?

Choice (Y/n):

Switching to the Registry File...

Some commands only work in certain files. For example, the EXPAND command can only be used to look at the index in a file which has an index. Enter "HELP COMMANDS" at an arrow prompt (=>) for a list of commands which can be used in this file.

=> FILE REGISTRY

COST IN U.S. DOLLARS

SINCE FILE

TOTAL

ENTRY

SESSION

FULL ESTIMATED COST

0.42

0.42

FILE 'REGISTRY' ENTERED AT 12:38:04 ON 09 MAY 2007

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TSCA INFORMATION NOW CURRENT THROUGH December 2, 2006

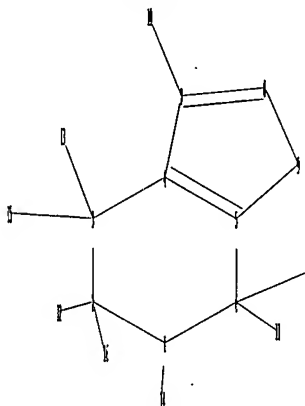
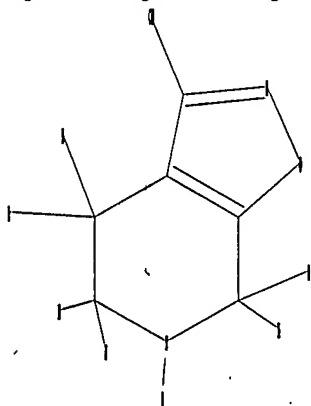
Please note that search-term pricing does apply when conducting SmartSELECT searches.

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<http://www.cas.org/support/stngen/stndoc/properties.html>

=>

Uploading C:\Program Files\Stnexp\Queries\10570551C.str



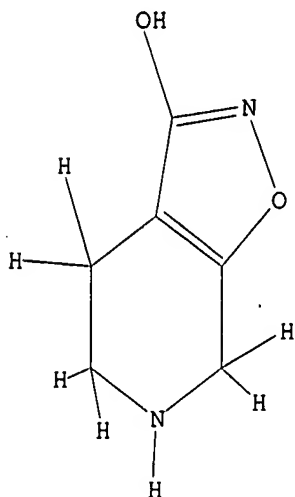
chain nodes :

10 11 12 13 14 15 16 17
 ring nodes :
 1 2 3 4 5 6 7 8 9
 chain bonds :
 1-14 2-12 2-16 3-13 3-15 6-11 6-17 7-10
 ring bonds :
 1-2 1-6 2-3 3-4 4-5 4-7 5-6 5-9 7-8 8-9
 exact/norm bonds :
 1-2 1-6 2-3 3-4 4-5 4-7 5-6 5-9 7-8 7-10 8-9
 exact bonds :
 1-14 2-12 2-16 3-13 3-15 6-11 6-17

Match level :
 1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:CLASS
 11:CLASS 12:CLASS 13:CLASS 14:CLASS 15:CLASS 16:CLASS 17:CLASS

L1 STRUCTURE UPLOADED

=> D L1
 L1 HAS NO ANSWERS
 L1 STR



Structure attributes must be viewed using STN Express query preparation.

=> s l1 full
 FULL SEARCH INITIATED 12:41:39 FILE 'REGISTRY'
 FULL SCREEN SEARCH COMPLETED - 261 TO ITERATE

 100.0% PROCESSED 261 ITERATIONS 36 ANSWERS
 SEARCH TIME: 00.00.01

L2 36 SEA SSS FUL L1

=> file caplus

| | | |
|----------------------|------------|---------|
| COST IN U.S. DOLLARS | SINCE FILE | TOTAL |
| | ENTRY | SESSION |
| FULL ESTIMATED COST | 174.35 | 174.77 |

FILE 'CAPLUS' ENTERED AT 12:41:50 ON 09 MAY 2007
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FILE COVERS 1907 - 9 May 2007 VOL 146 ISS 20
FILE LAST UPDATED: 8 May 2007 (20070508/ED)

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<http://www.cas.org/infopolicy.html>

```
=> s l2/prep full
      481 L2
      4400083 PREP/RL
L3      13 L2/PREP
      (L2 (L) PREP/RL)
```

```
=> s l3 and nucleo?
      742508 NUCLEO?
L4      0 L3 AND NUCLEO?
```

```
=> d ibib abs hitstr l3 tot
```

L3 ANSWER 1 OF 13 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2006:1177390 CAPLUS
DOCUMENT NUMBER: 145:495605
TITLE: Acid and base salt forms of gaboxadol
INVENTOR(S): Crocker, Louis S.; Murry, Jerry A.; Nagapudi, Karthik;
Rubin, Kara Beth
PATENT ASSIGNEE(S): Merck & Co., Inc., USA
SOURCE: PCT Int. Appl., 20pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---------------|--|----------|-----------------|----------|
| WO 2006118897 | A1 | 20061109 | WO 2006-US15789 | 20060425 |
| W: | AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | |
| RW: | AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | |

PRIORITY APPLN. INFO.: US 2005-676332P P 20050429
AB The present invention is directed to novel acid salt forms and base salt

forms of the compound gaboxadol (4,5,6,7-tetrahydroisoxazolo[5,4-c]pyridin-3-ol) and hydrates, solvates and polymorphic forms thereof. The invention is further concerned with pharmaceutical compns. containing the salt forms as an active ingredient, methods for treatment of disorders susceptible to amelioration by GABAA receptor agonism with the salt forms, and processes for the preparation of the salt forms.

IT 914291-56-8P 914291-57-9P 914291-58-0P
914291-59-1P 914291-60-4P 914291-62-6P
914291-64-8P 914291-66-0P 914291-67-1P
914291-68-2P 914291-69-3P 914291-71-7P
914291-72-8P 914291-73-9P

RL: PEP (Physical, engineering or chemical process); PYP (Physical process); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)

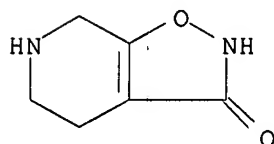
(acid and base salt forms of gaboxadol)

RN 914291-56-8 CAPLUS

CN Isoxazolo[5,4-c]pyridin-3(2H)-one, 4,5,6,7-tetrahydro-, monoacetate (9CI)
(CA INDEX NAME)

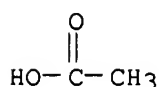
CM 1

CRN 64603-91-4
CMF C6 H8 N2 O2



CM 2

CRN 64-19-7
CMF C2 H4 O2

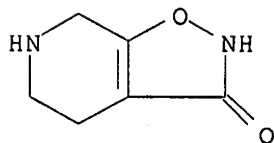


RN 914291-57-9 CAPLUS

CN Isoxazolo[5,4-c]pyridin-3(2H)-one, 4,5,6,7-tetrahydro-,
2-hydroxy-1,2,3-propanetricarboxylate (3:1) (9CI) (CA INDEX NAME)

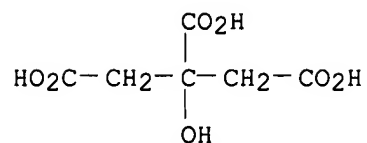
CM 1

CRN 64603-91-4
CMF C6 H8 N2 O2



CM 2

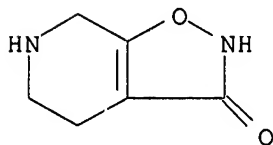
CRN 77-92-9
CMF C6 H8 O7



RN 914291-58-0 CAPLUS
CN Isoxazolo[5,4-c]pyridin-3(2H)-one, 4,5,6,7-tetrahydro-,
(2E)-2-butenedioate (2:1) (9CI) (CA INDEX NAME)

CM 1

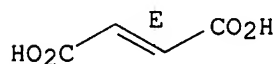
CRN 64603-91-4
CMF C6 H8 N2 O2



CM 2

CRN 110-17-8
CMF C4 H4 O4

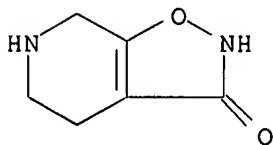
Double bond geometry as shown.



RN 914291-59-1 CAPLUS
CN Isoxazolo[5,4-c]pyridin-3(2H)-one, 4,5,6,7-tetrahydro-, phosphate (3:1)
(9CI) (CA INDEX NAME)

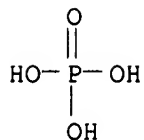
CM 1

CRN 64603-91-4
CMF C6 H8 N2 O2



CM 2

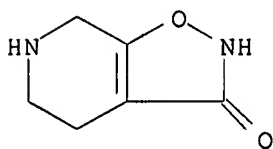
CRN 7664-38-2
CMF H3 O4 P



RN 914291-60-4 CAPLUS
 CN Isoxazolo[5,4-c]pyridin-3(2H)-one, 4,5,6,7-tetrahydro-,
 (2R,3R)-2,3-dihydroxybutanedioate (2:1) (9CI) (CA INDEX NAME)

CM 1

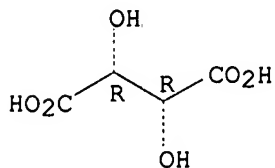
CRN 64603-91-4
 CMF C6 H8 N2 O2



CM 2

CRN 87-69-4
 CMF C4 H6 O6

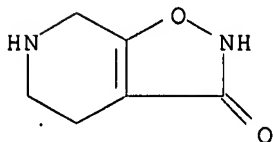
Absolute stereochemistry.



RN 914291-62-6 CAPLUS
 CN Butanedioic acid, compd. with 4,5,6,7-tetrahydroisoxazolo[5,4-c]pyridin-
 3(2H)-one (1:2) (9CI) (CA INDEX NAME)

CM 1

CRN 64603-91-4
 CMF C6 H8 N2 O2



CM 2

CRN 110-15-6
 CMF C4 H6 O4

HO₂C-CH₂-CH₂-CO₂H

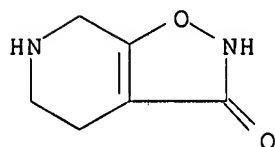
RN 914291-64-8 CAPLUS

CN Isoxazolo[5,4-c]pyridin-3(2H)-one, 4,5,6,7-tetrahydro-, sulfate (2:1)
(9CI) (CA INDEX NAME)

CM 1

CRN 64603-91-4

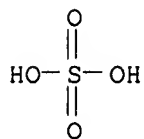
CMF C6 H8 N2 O2



CM 2

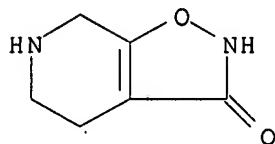
CRN 7664-93-9

CMF H2 O4 S



RN 914291-66-0 CAPLUS

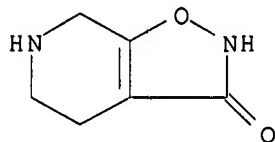
CN Isoxazolo[5,4-c]pyridin-3(2H)-one, 4,5,6,7-tetrahydro-, calcium salt (2:1)
(9CI) (CA INDEX NAME)



● 1/2 Ca

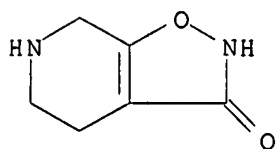
RN 914291-67-1 CAPLUS

CN Isoxazolo[5,4-c]pyridin-3(2H)-one, 4,5,6,7-tetrahydro-, monopotassium salt
(9CI) (CA INDEX NAME)



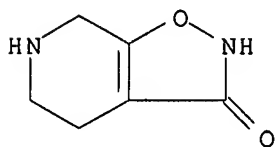
● K

RN 914291-68-2 CAPLUS
CN Isoxazolo[5,4-c]pyridin-3(2H)-one, 4,5,6,7-tetrahydro-, magnesium salt
(2:1) (9CI) (CA INDEX NAME)



● 1/2 Mg

RN 914291-69-3 CAPLUS
CN Isoxazolo[5,4-c]pyridin-3(2H)-one, 4,5,6,7-tetrahydro-, monosodium salt
(9CI) (CA INDEX NAME)

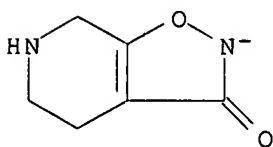


● Na

RN 914291-71-7 CAPLUS
CN Ethanaminium, 2-hydroxy-N,N,N-trimethyl-, salt with 4,5,6,7-tetrahydroisoxazolo[5,4-c]pyridin-3(2H)-one (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 914291-70-6
CMF C6 H7 N2 O2



CM 2

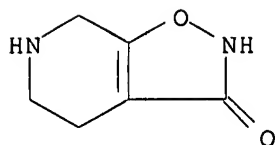
CRN 62-49-7
CMF C5 H14 N O

Me₃⁺N-CH₂-CH₂-OH

RN 914291-72-8 CAPLUS
CN L-Lysine, compd. with 4,5,6,7-tetrahydroisoxazolo[5,4-c]pyridin-3(2H)-one
(1:1) (9CI) (CA INDEX NAME)

CM 1

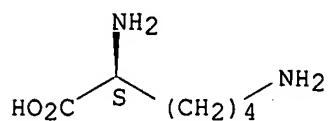
CRN 64603-91-4
CMF C6 H8 N2 O2



CM 2

CRN 56-87-1
CMF C6 H14 N2 O2

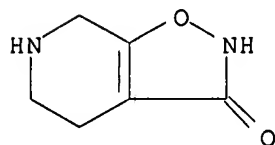
Absolute stereochemistry.



RN 914291-73-9 CAPLUS
CN Isoxazolo[5,4-c]pyridin-3(2H)-one, 4,5,6,7-tetrahydro-, compd. with
N,N-bis(phenylmethyl)-1,2-ethanediamine (1:1) (9CI) (CA INDEX NAME)

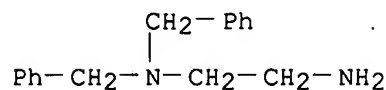
CM 1

CRN 64603-91-4
CMF C6 H8 N2 O2



CM 2

CRN 14165-27-6
CMF C16 H20 N2



REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 2 OF 13 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2006:1009629 CAPLUS
DOCUMENT NUMBER: 145:383399
TITLE: Gaboxadol forms, compositions thereof, methods for
preparation and uses for treating sleep disorders
INVENTOR(S): Almarsson, Orn; Hickey, Magali Bourghol; Peterson,
Matthew

PATENT ASSIGNEE(S): Transform Pharmaceuticals, Inc., USA
 SOURCE: PCT Int. Appl., 56pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------|----------|-----------------|----------|
| WO 2006102093 | A1 | 20060928 | WO 2006-US9737 | 20060317 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |

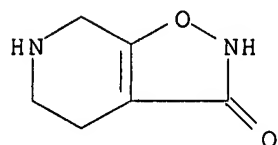
PRIORITY APPLN. INFO.: US 2005-663423P P 20050318

AB The invention provides novel gaboxadol forms and methods for making and using the same. These forms include salts, hydrates, solvates, and polymorphs of gaboxadol with improved aqueous solubility when compared to known gaboxadol forms. The invention also provides novel compounds comprising these novel soluble forms and a suitable carrier. The invention also provides related methods of treatment. Compounds and methods of the invention of the invention have a number of uses, including the treatment or prevention of sleep disorders.

IT 815574-58-4P, Gaboxadol monohydrate 910641-51-9P
 RL: PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use);
 BIOL (Biological study); PREP (Preparation); USES (Uses)
 (gaboxadol forms, compounds thereof, methods for preparation and uses for treating sleep disorders)

RN 815574-58-4 CAPLUS

CN Isoxazolo[5,4-c]pyridin-3(2H)-one, 4,5,6,7-tetrahydro-, monohydrate (9CI)
 (CA INDEX NAME)



● H₂O

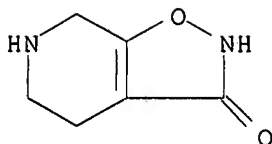
RN 910641-51-9 CAPLUS

CN Isoxazolo[5,4-c]pyridin-3(2H)-one, 4,5,6,7-tetrahydro-,
 (2Z)-2-butenedioate (9CI) (CA INDEX NAME)

CM 1

CRN 64603-91-4

CMF C6 H8 N2 O2

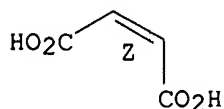


CM 2

CRN 110-16-7

CMF C4 H4 O4

Double bond geometry as shown.



IT 64603-91-4P, Gaboxadol

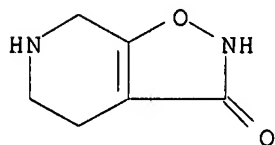
RL: RCT (Reactant); SPN (Synthetic preparation); PREP

(Preparation); RACT (Reactant or reagent)

(gaboxadol forms, compns. thereof, methods for preparation and uses for treating sleep disorders)

RN 64603-91-4 CAPLUS

CN Isoxazolo[5,4-c]pyridin-3(2H)-one, 4,5,6,7-tetrahydro- (CA INDEX NAME)



REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 3 OF 13 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2006:795633 CAPLUS

DOCUMENT NUMBER: 145:217970

TITLE: Polymorphic forms of a GABA agonist

INVENTOR(S): Kumke, Daniel J.; Murry, Jerry A.; Simmons, Bryon L.; Xu, Feng

PATENT ASSIGNEE(S): Merck & Co., Inc., USA

SOURCE: PCT Int. Appl., 12pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---------------|------|----------|-----------------|----------|
| WO 2006083682 | A2 | 20060810 | WO 2006-US2809 | 20060126 |
| WO 2006083682 | A3 | 20070405 | | |

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC,

VN, YU, ZA, ZM, ZW
 RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE,
 IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ,
 CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH,
 GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
 KG, KZ, MD, RU, TJ, TM, AP, EA, EP, OA

PRIORITY APPLN. INFO.: US 2005-648151P P 20050128

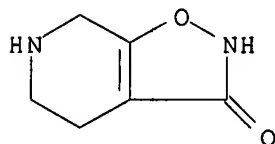
AB The present invention is directed to novel polymorphic forms of 4,5,6,7-tetrahydroisoxazolo[5,4-c]pyridin-3-ol hydrate (gaboxadol monohydrate). The invention is further concerned with pharmaceutical compns. containing the polymorphic forms as an active ingredient, methods for treatment of disorders susceptible to amelioration by GABAA receptor agonism with the polymorphic forms, and processes for the preparation of the polymorphic forms. Gaboxadol-HCl was dissolved in water-isopropanol and was treated with 1 equiv of 5N NaOH. The solution was stirred and the slurry was aged for hours at ambient temperature. The resulting white solid was filtered and air dried to give the gaboxadol monohydrate form III.

IT 815574-58-4P, Gaboxadol monohydrate

RL: PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses) (polymorphic forms of GABA agonist)

RN 815574-58-4 CAPLUS

CN Isoxazolo[5,4-c]pyridin-3(2H)-one, 4,5,6,7-tetrahydro-, monohydrate (9CI) (CA INDEX NAME)



● H₂O

L3 ANSWER 4 OF 13 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2005:686172 CAPLUS

DOCUMENT NUMBER: 143:179592

TITLE: Crystalline forms of a GABAA agonist, gaboxadol for treatment of neurological and psychiatric disorders

INVENTOR(S): Cooper, Vincent Brett

PATENT ASSIGNEE(S): Merck Sharp & Dohme Limited, UK

SOURCE: Brit. UK Pat. Appl., 19 pp.

CODEN: BAXXDU

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|--|------|----------|-----------------|----------|
| ----- | ---- | ----- | ----- | ----- |
| GB 2410434 | A | 20050803 | GB 2005-1847 | 20050128 |
| US 2005171142 | A1 | 20050804 | US 2005-45768 | 20050128 |
| AU 2005209473 | A1 | 20050811 | AU 2005-209473 | 20050128 |
| CA 2554536 | A1 | 20050811 | CA 2005-2554536 | 20050128 |
| WO 2005073237 | A2 | 20050811 | WO 2005-GB288 | 20050128 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, | | | | |
| CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, | | | | |
| GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, | | | | |
| LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, | | | | |
| NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, | | | | |

TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
 RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM,
 AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK,
 EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT,
 RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML,
 MR, NE, SN, TD, TG

EP 1713813 A2 20061025 EP 2005-702040 20050128
 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
 IE, SI, LT, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK, IS

CN 1914212 A 20070214 CN 2005-80003161 20050128
 NO 2006003843 A 20060829 NO 2006-3843 20060829

PRIORITY APPLN. INFO.: GB 2004-2118 A 20040130
 WO 2005-GB288 W 20050128

AB Two new crystalline monohydrates and two new crystalline anhydrides of gaboxadol are disclosed together with methods for preparing them. The methods comprise dissolving an acid salt of gaboxadol in water, adjusting the pH to pH 6.5 and either collecting the precipitate immediately or allowing it to age for 12

h.
 The crystalline gaboxadol is intended for use in the treatment of neurol. or psychiatric disorders susceptible to amelioration by GABAA receptor agonist. Thus, a solution of gaboxadol hydrochloride was treated with sufficient triethylamine to give a pH of 6.5. The resulting white solid was collected, filtered and air dried giving gaboxadol monohydrate Form I.

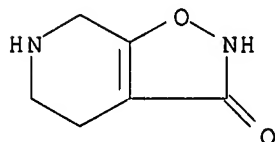
IT 815574-58-4P

RL: PNU (Preparation, unclassified); PRP (Properties); RCT (Reactant); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)

(crystalline forms of gaboxadol for dosage forms for treatment of neurol. or psychiatric disorders susceptible to amelioration by GABAA receptor agonism)

RN 815574-58-4 CAPLUS

CN Isoxazolo[5,4-c]pyridin-3(2H)-one, 4,5,6,7-tetrahydro-, monohydrate (9CI)
 (CA INDEX NAME)



● H2O

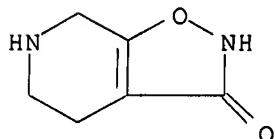
IT 64603-91-4P, Gaboxadol

RL: PNU (Preparation, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(crystalline forms of gaboxadol for dosage forms for treatment of neurol. or psychiatric disorders susceptible to amelioration by GABAA receptor agonism)

RN 64603-91-4 CAPLUS

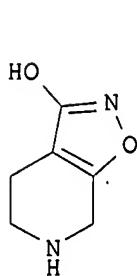
CN Isoxazolo[5,4-c]pyridin-3(2H)-one, 4,5,6,7-tetrahydro- (CA INDEX NAME)



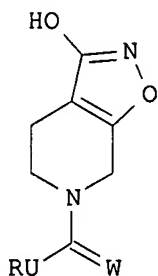
REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 5 OF 13 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:238996 CAPLUS
DOCUMENT NUMBER: 142:316828
TITLE: Method for the manufacture of THIP
INVENTOR(S): Petersen, Hans; Bech Sommer, Michael; Dancer, Robert
PATENT ASSIGNEE(S): H. Lundbeck A/S, Den.
SOURCE: PCT Int. Appl., 34 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------|----------|--|------------|
| WO 2005023820 | A1 | 20050317 | WO 2004-DK579 | 20040901 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | | |
| RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| AU 2004270323 | A1 | 20050317 | AU 2004-270323 | 20040901 |
| CA 2537840 | A1 | 20050317 | CA 2004-2537840 | 20040901 |
| EP 1664060 | A1 | 20060607 | EP 2004-762799 | 20040901 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, HR | | | | |
| CN 1845928 | A | 20061011 | CN 2004-80025424 | 20040901 |
| BR 2004013741 | A | 20061024 | BR 2004-13741 | 20040901 |
| JP 2007504179 | T | 20070301 | JP 2006-525046 | 20040901 |
| NO 2006001424 | A | 20060329 | NO 2006-1424 | 20060329 |
| PRIORITY APPLN. INFO.: | | | DK 2003-1277 | A 20030905 |
| | | | US 2003-500422P | P 20030905 |
| | | | WO 2004-DK579 | W 20040901 |
| OTHER SOURCE(S): | | | CASREACT 142:316828; MARPAT 142:316828 | |
| GI | | | | |



I



II

AB The present invention relates to a new method of preparing gaboxadol (THIP; I), which is useful for treating sleep disorders (no data). In particular a method of preparing THIP comprising reacting a compound II [R = alkyl, cycloalkyl, aryl, etc.; U = N, CR1 (R1 = H, R); W = O, S, NR4 (R4 = H, R)]

or a salt thereof with an acid, typically a mineral acid, to obtain THIP as an acid addition salt. The present invention also relates to several intermediates. E.g., a multi-step synthesis of I.HBr, starting from Me 3-hydroxyisonicotinate, was given.

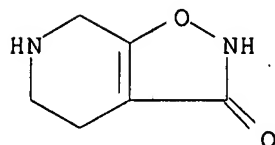
IT 65202-63-3P

RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)

(method for the manufacture of THIP)

RN 65202-63-3 CAPLUS

CN Isoxazolo[5,4-c]pyridin-3(2H)-one, 4,5,6,7-tetrahydro-, monohydrobromide (9CI) (CA INDEX NAME)



● HBr

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 6 OF 13 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2004:720824 CAPLUS

DOCUMENT NUMBER: 141:306879

TITLE: Gaboxadol (Lundbeck/Merck)

AUTHOR(S): Huckle, Richard

CORPORATE SOURCE: Innovation Center, Actelion Ltd, Allschwil, CH-4123, Switz.

SOURCE: Current Opinion in Investigational Drugs (Thomson Scientific) (2004), 5(7), 766-773
CODEN: COIDAZ; ISSN: 1472-4472

PUBLISHER: Thomson Scientific

DOCUMENT TYPE: Journal; General Review

LANGUAGE: English

AB A review. H Lundbeck A/S, in collaboration with Merck & Co Inc, is developing gaboxadol, a GABAA agonist, for the potential treatment of sleep disorders. The compound is currently undergoing phase III clin. trials.

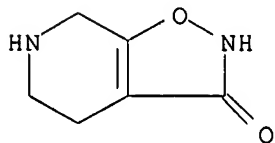
IT 64603-91-4P, Gaboxadol

RL: ADV (Adverse effect, including toxicity); DMA (Drug mechanism of action); PAC (Pharmacological activity); PKT (Pharmacokinetics); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(GABAA agonist gaboxadol for potential treatment of sleep disorders)

RN 64603-91-4 CAPLUS

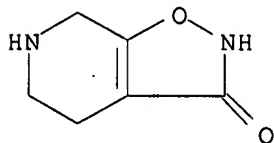
CN Isoxazolo[5,4-c]pyridin-3(2H)-one, 4,5,6,7-tetrahydro- (CA INDEX NAME)



REFERENCE COUNT: 64 THERE ARE 64 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 7 OF 13 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1995:726673 CAPLUS
 DOCUMENT NUMBER: 123:169581
 TITLE: Partial GABAA Receptor Agonists. Synthesis and in Vitro Pharmacology of a Series of Nonannulated Analogs of 4,5,6,7-Tetrahydroisoxazolo[4,5-c]pyridin-3-ol
 AUTHOR(S): Frolund, Bente; Kristiansen, Uffe; Brehm, Lotte; Hansen, Annette B.; Krogsgaard-Larsen, Povl; Falch, Erik
 CORPORATE SOURCE: PharmaBiotec Research Center, Royal Danish School of Pharmacy, Copenhagen, DK-2100, Den.
 SOURCE: Journal of Medicinal Chemistry (1995), 38(17), 3287-96
 CODEN: JMCMAR; ISSN: 0022-2623
 PUBLISHER: American Chemical Society
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 OTHER SOURCE(S): CASREACT 123:169581
 AB 5-(4-Piperidinyl)3-isoxazolol (4-PIOL), a structural analog of 4-aminobutanoic acid (GABA) and the GABAA agonist 4,5,6,7-tetrahydroisoxazolo[5,4-c]pyridin-3-ol (THIP), is a low-efficacy partial GABAA agonist. A number of compds. bioisosterically derived from 4-PIOL, including 5-(4-piperidinyl)-3-isothiazolol, 3-(4-piperidinyl)-5-isoxazolol 5-(1,2,3,6-tetrahydropyrid-4-yl)-3-isoxazolol, and 5-(1,2,3,6-tetrahydropyrid-4-yl)isothiazol-3-ol, were synthesized and tested as GABAA receptor ligands. Whereas none of these compds. significantly affected GABAB receptor binding or GABA uptake, they showed affinities for GABAA receptor sites in the low-micromolar range. Using cultured cerebral cortical neurons and whole-cell patch-clamp techniques, the efficacies of these compds. relative to that of the full GABAA agonist, isoguvacine (20 μ M), were determined. The relative efficacy of 5-(4-piperidinyl)-3-isothiazolol, which has a higher receptor affinity ($IC_{50} = 1.3 \mu$ M) than 4-PIOL ($IC_{50} = 9.3 \mu$ M), was comparable with that of 4-PIOL (30-35%). The tetrahydropyridine analog of 4-PIOL, compound 5-(1,2,3,6-tetrahydropyrid-4-yl)-3-isoxazolol, showed a markedly lower receptor affinity ($IC_{50} = 32 \mu$ M) and apparently a lower relative efficacy than 4-PIOL. The corresponding unsatd. analog of 5-(4-piperidinyl)-3-isothiazolol, compound 14, showed a slightly weaker receptor affinity ($IC_{50} = 4.0 \mu$ M) but a significantly higher relative efficacy (50-55%) than 5-(4-piperidinyl)-3-isothiazolol. The 5-isoxazolol isomer of 4-PIOL, compound 3-(4-piperidinyl)-5-isoxazolol, showed a reduced receptor affinity ($IC_{50} = 26 \mu$ M) and a very low relative efficacy. Substitution of propanoic or propenoic acid moieties for the acidic heterocyclic units of these compds. gave the monocyclic amino acid derivs., which have very little or no affinity for GABAA receptor sites.
 IT 64603-91-4DP, Isoxazolo[5,4-c]pyridin-3(2H)-one, 4,5,6,7-tetrahydro, analogs
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
 (THIP; preparation of isoxazolo[5,4-c]pyridinone analogs as GABAa agonists)
 RN 64603-91-4 CAPLUS
 CN Isoxazolo[5,4-c]pyridin-3(2H)-one, 4,5,6,7-tetrahydro-, (CA INDEX NAME)



TITLE: 3-Hydroxyisoxazole bioisosteres of GABA. Synthesis of a series of 4-substituted muscimol analogs and identification of a bicyclic 2-isoxazoline rearrangement product

AUTHOR(S): Hjeds, Hans; Christensen, Inge T.; Cornett, Claus; Froelund, Bente; Falch, Erik; Pedersen, Joergen B.; Krosgaard-Larsen, Povl

CORPORATE SOURCE: PharmaBiotec Res. Cent., R. Dan. Sch. Pharm., Copenhagen, DK-2100, Den.

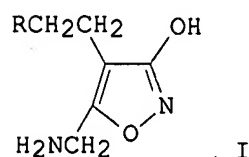
SOURCE: Acta Chemica Scandinavica (1992), 46(8), 772-7
CODEN: ACHSE7; ISSN: 0904-213X

DOCUMENT TYPE: Journal

LANGUAGE: English

OTHER SOURCE(S): CASREACT 117:191577

GI

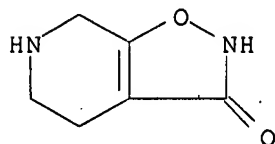


AB 3-Hydroxy-4-(2-hydroxyethyl)-5-methylisoxazole was used as the starting material for the syntheses of the muscimol analogs I (R = OH, Cl, OAc). Whilst muscimol is a very potent agonist at GABAA receptors, I did not show significant affinity for GABAA receptor sites in vitro.

IT 65202-63-3P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

RN 65202-63-3 CAPLUS

CN Isoxazolo[5,4-c]pyridin-3(2H)-one, 4,5,6,7-tetrahydro-, monohydrobromide (9CI) (CA INDEX NAME)



● HBr

L3 ANSWER 9 OF 13 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1984:465548 CAPLUS

DOCUMENT NUMBER: 101:65548

TITLE: Analgesic GABA agonists. Synthesis and structure-activity studies on analogs and derivatives of muscimol and THIP

AUTHOR(S): Haeffliger, Walter; Revesz, Laszlo; Maurer, Richard; Roemer, Dietmar; Buescher, Heinz Hermann

CORPORATE SOURCE: Sandoz Ltd., Basel, CH-4002, Switz.

SOURCE: European Journal of Medicinal Chemistry (1984), 19(2), 149-56
CODEN: EJMCA5; ISSN: 0009-4374

DOCUMENT TYPE: Journal

LANGUAGE: English

OTHER SOURCE(S): CASREACT 101:65548

AB A series of analogs. and derivs. (prodrugs) of muscimol and THIP were prepared and their GABA receptor affinity, analgesic, and GABAergic properties examined. Some compds. designed as prodrugs exhibited high GABA receptor affinity indicating that nonzwitterionic mols. interact with GABA receptors. Analgesic and GABAergic activities of muscimol prodrugs were pronounced but weaker than muscimol itself. A ring opened THIP derivative was inactive whereas its carbamate derivative showed analgesic and GABAergic activity. A benzophenone-imine derivative showed strong GABA binding but no analgesic activity. Carbamate type THIP prodrugs were also active in analgesic and anticonvulsive tests but weaker than THIP itself. Ester- and alkanoyloxymethyl prodrugs were only active in the hot plate test. When the inactive 7-methyl-THIP was converted to a potential prodrug it produced high GABA-mimetic activity in both anticonvulsant and analgesic tests. In all cases, sedation was inseparable from analgesia.

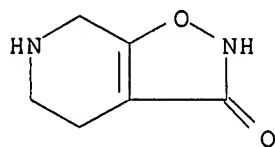
IT 64603-91-4DP, derivs.

RL: SPN (Synthetic preparation); PREP (Preparation)

(preparation and GABA agonist activity of, mol. structure in relation to)

RN 64603-91-4 CAPLUS

CN Isoxazolo[5,4-c]pyridin-3(2H)-one, 4,5,6,7-tetrahydro- (CA INDEX NAME)



L3 ANSWER 10 OF 13 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1982:562964 CAPLUS

DOCUMENT NUMBER: 97:162964

TITLE: Isoxazolo[5,4-c]pyridines which are GABA-agonists

INVENTOR(S): Krogsgaard-Larsen, Povl

PATENT ASSIGNEE(S): Lundbeck, H., og Co. A/S, Den.

SOURCE: Can., 29 pp. Division of Can. Appl. No. 305,798.

CODEN: CAXXA4

DOCUMENT TYPE: Patent

LANGUAGE: English

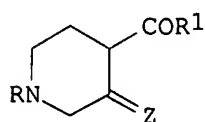
FAMILY ACC. NUM. COUNT: 3

PATENT INFORMATION:

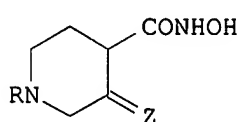
| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------------------|------|----------|-----------------|-------------|
| CA 1125288 | A2 | 19820608 | CA 1981-377128 | 19810507 |
| CA 1107736 | A1 | 19810825 | CA 1978-305798 | 19780620 |
| US 4301287 | A | 19811117 | US 1979-104080 | 19791217 |
| PRIORITY APPLN. INFO.: | | | GB 1977-25740 | A 19770620 |
| | | | CA 1978-305798 | A3 19780620 |
| | | | US 1978-917118 | A3 19780619 |

OTHER SOURCE(S): MARPAT 97:162964

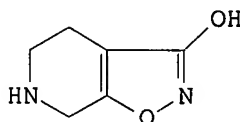
GI



I



II



III

AB Piperidinecarboxylic acid compds. I (R = Ac, carbalkoxy, carbophenoxy, CPh3, CHO; Z = ketalized O; R1 = halo, OH, alkoxy) reacted with HONH2 to

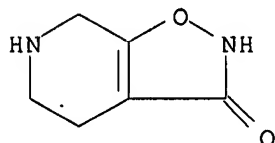
yield hydroxamic acids II. Isoxazolo[5,4-c]pyridine derivative III, which is an agonist of $\text{H}_2\text{N}(\text{CH}_2)_3\text{CO}_2\text{H}$, was prepared from II. I ($\text{R} = \text{CO}_2\text{Me}$, $\text{R}_1 = \text{OEt}$, $\text{Z} = \text{OCH}_2\text{CH}_2\text{O}$) reacted with HONH_2 to give II ($\text{R} = \text{CO}_2\text{Me}$, $\text{Z} = \text{OCH}_2\text{CH}_2\text{O}$), and the latter was treated with HCl and then with $\text{HBr}\cdot\text{HOAc}$ to give III.HBr.

IT 64603-91-4P 65202-63-3P

RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation and use of, as gamma-aminobutyric acid agonist)

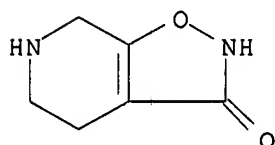
RN 64603-91-4 CAPLUS

CN Isoxazolo[5,4-c]pyridin-3(2H)-one, 4,5,6,7-tetrahydro- (CA INDEX NAME)



RN 65202-63-3 CAPLUS

CN Isoxazolo[5,4-c]pyridin-3(2H)-one, 4,5,6,7-tetrahydro-, monohydrobromide
(9CI) (CA INDEX NAME)



● HBr

L3 ANSWER 11 OF 13 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1982:527546 CAPLUS

DOCUMENT NUMBER: 97:127546

TITLE: Deuterium labeling of the GABA agonists THIP,
piperidine-4-sulfonic acid, and the GABA uptake
inhibitor THPO

AUTHOR(S): Krogsgaard-Larsen, Povl; Johansen, Joergen Stage;
Falch, Erik

CORPORATE SOURCE: Dep. Chem. BC, R. Dan. Sch. Pharm., Copenhagen,
DK-2100, Den.

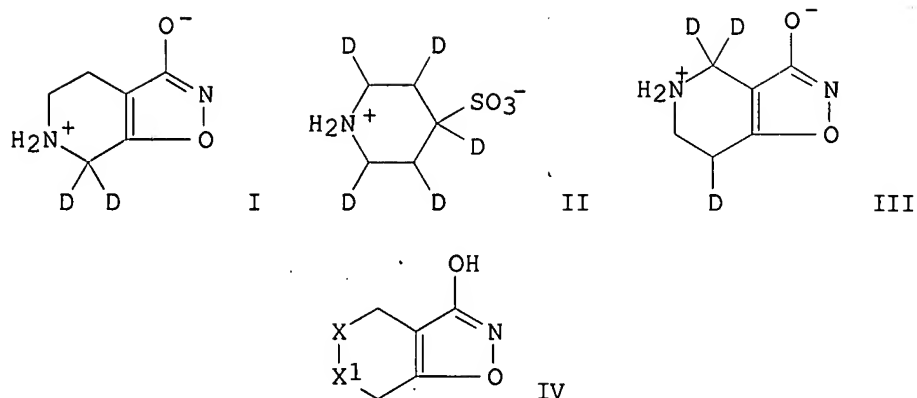
SOURCE: Journal of Labelled Compounds and Radiopharmaceuticals
(1982), 19(5), 689-702

CODEN: JLCRD4; ISSN: 0362-4803

DOCUMENT TYPE: Journal

LANGUAGE: English

GI

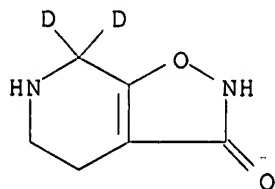


AB The D-labeled title compds. (I, II, and III, resp.) were prepared I and III were prepared from IV (X = CH₂, X₁ = NCO₂Me; X = NCO₂Me, X₁ = CH₂), resp., by sequential methylation, N-decarboxylation, nitrosation, H-D exchange reaction with D₂O (acid- and base-catalyzed, resp.), denitrosation, and demethylation. Pt-catalyzed deuteration of pyridine-4-sulfonic acid in D₂O gave II.

IT 82988-63-4P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

RN 82988-63-4 CAPLUS

CN Isoxazolo[5,4-c]pyridin-3(2H)-one-7-d, 4,5,6,7-tetrahydro-7-d- (9CI) (CA INDEX NAME)



L3 ANSWER 12 OF 13 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1979:439458 CAPLUS

DOCUMENT NUMBER: 91:39458

TITLE: Methyl tetrahydrohydroxy isoxazolopyridine carboxylate

INVENTOR(S): Krogsgaard-Larsen, Povl

PATENT ASSIGNEE(S): Den.

SOURCE: Jpn. Kokai Tokkyo Koho, 13 pp.
CODEN: JKXXAF

DOCUMENT TYPE: Patent

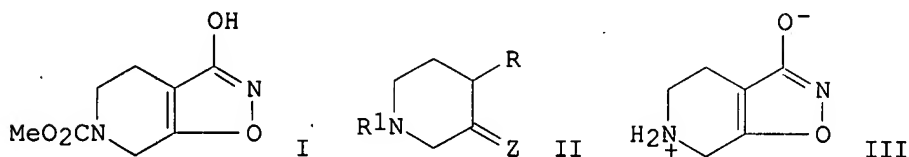
LANGUAGE: Japanese

FAMILY ACC. NUM. COUNT: 3

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|-------------|------|----------|-----------------|----------|
| JP 54036290 | A | 19790316 | JP 1978-74800 | 19780620 |
| DK 7802702 | A | 19781221 | DK 1978-2702 | 19780615 |
| DK 7802703 | A | 19781221 | DK 1978-2703 | 19780615 |
| FI 7801954 | A | 19781221 | FI 1978-1954 | 19780619 |
| FI 64376 | B | 19830729 | | |
| FI 64376 | C | 19831110 | | |
| FI 7801955 | A | 19781221 | FI 1978-1955 | 19780619 |
| NO 7802127 | A | 19781221 | NO 1978-2127 | 19780619 |

| | | | | |
|-----------------------------------|----|----------|-----------------|-------------|
| NO 152049 | B | 19850415 | | |
| NO 152449 | C | 19850724 | | |
| NO 7802128 | A | 19781221 | NO 1978-2128 | 19780619 |
| EP 167 | A1 | 19790110 | EP 1978-100190 | 19780619 |
| R: BE, CH, DE, FR, GB, LU, NL, SE | | | | |
| EP 338 | A2 | 19790124 | EP 1978-100191 | 19780619 |
| EP 338 | A3 | 19790627 | | |
| EP 338 | B1 | 19811125 | | |
| R: BE, CH, DE, FR, GB, LU, NL, SE | | | | |
| ES 470912 | A1 | 19790201 | ES 1978-470912 | 19780619 |
| ES 470913 | A1 | 19790201 | ES 1978-470913 | 19780619 |
| ZA 7803492 | A | 19790627 | ZA 1978-3492 | 19780619 |
| ZA 7803493 | A | 19790627 | ZA 1978-3493 | 19780619 |
| AU 7837244 | A | 19800103 | AU 1978-37244 | 19780619 |
| US 4278676 | A | 19810714 | US 1978-917118 | 19780619 |
| AU 7837298 | A | 19800103 | AU 1978-37298 | 19780620 |
| AU 521040 | B2 | 19820311 | | |
| AT 7804486 | A | 19820215 | AT 1978-4486 | 19780620 |
| AT 368505 | B | 19821025 | | |
| NO 7902839 | A | 19781221 | NO 1979-2839 | 19790903 |
| US 4301287 | A | 19811117 | US 1979-104080 | 19791217 |
| EP 27279 | A1 | 19810422 | EP 1980-106497 | 19801023 |
| R: BE, CH, DE, FR, GB, LU, NL, SE | | | | |
| EP 28017 | A1 | 19810506 | EP 1980-106498 | 19801023 |
| R: BE, CH, DE, FR, GB, LU, NL, SE | | | | |
| PRIORITY APPLN. INFO.: | | | GB 1977-25740 | A 19770620 |
| | | | US 1978-917118 | A3 19780619 |
| OTHER SOURCE(S): | | | MARPAT 91:39458 | |
| GI | | | | |



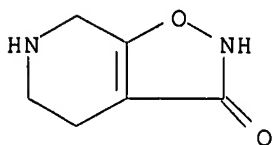
AB The title compound (I) was prepared Thus, (methoxycarbonyl)piperidinone II (R = CO₂Et, R₁ = CO₂Me, Z = O) [obtained by hydrogenating II (R = CO₂Et, R₁ = CH₂Ph, Z = O) over Pd-C, and reacting the product with ClCO₂Me] was ketalized with HOCH₂CH₂OH to give the ethylene acetal II (R = CO₂Et, R₁ = CO₂Me, Z = OCH₂CH₂O), which was treated with H₂NOH.HCl to give II (R = CONHOH, R₁ = CO₂Me, Z = OCH₂CH₂O), whose cyclization in H₂SO₄ gave the hydroxyisoxazolopiperidinecarboxylate. Decarboxylation of I followed by treatment with HBr and then H₂O-Et₃N-EtOH gave zwitterion III. III was a mild tranquilizer in mice.

IT 64603-91-4P

RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation and tranquilizing activity of)

RN 64603-91-4 CAPLUS

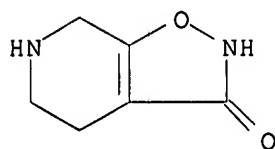
CN Isoxazolo[5,4-c]pyridin-3(2H)-one, 4,5,6,7-tetrahydro- (CA INDEX NAME)



IT 65202-63-3P

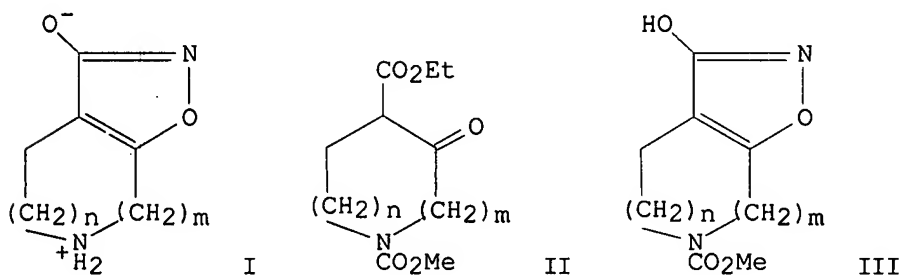
RL: SPN (Synthetic preparation); PREP (Preparation)

(preparation of)
 RN 65202-63-3 CAPLUS
 CN Isoxazolo[5,4-c]pyridin-3(2H)-one, 4,5,6,7-tetrahydro-, monohydrobromide
 (9CI) (CA INDEX NAME)



● HBr

L3 ANSWER 13 OF 13 CAPLUS COPYRIGHT 2007 ACS on STN
 ACCESSION NUMBER: 1978:37672 CAPLUS
 DOCUMENT NUMBER: 88:37672
 TITLE: Muscimol analogs. II. Synthesis of some bicyclic
 3-isoxazolol zwitterions
 AUTHOR(S): Krogsgaard-Larsen, Povl
 CORPORATE SOURCE: Dep. Chem. BC, R. Dan. Sch. Pharm., Copenhagen, Den.
 SOURCE: Acta Chemica Scandinavica, Series B: Organic
 Chemistry and Biochemistry (1977), B31(7), 584-8
 CODEN: ACBOCV; ISSN: 0302-4369
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 OTHER SOURCE(S): CASREACT 88:37672
 GI



AB The 3-isoxazolol zwitterions 4,5,6,7-tetrahydroisoxazolo[5,4-c]pyridin-3-ol, (I, n = 1, m = 1), 5,6,7,8-tetrahydro-4H-isoxazolo[5,4-c]azepin-3-ol (I, n = 2, m = 1), and 5,6,7,8-tetrahydro-4H-isoxazolo[4,5-c]azepin-3-ol (I, n = 0, m = 3) were prepared. The starting materials were the cyclic β -oxoesters II. The ethylene acetals of II were treated with HONH₂ followed by deacetalization and cyclization of the intermediate β -oxohydroxamic acid ethylene acetals to give the resp. 3-isoxazolol derivs. III, which were transformed into the zwitterions I. The pK_a values of I were determined.

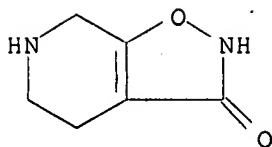
IT 65202-63-3P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP
 (Preparation); RACT (Reactant or reagent)

(preparation and reaction with triethylamine, zwitterions from)

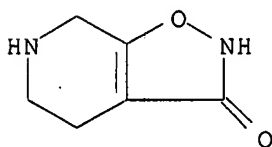
RN 65202-63-3 CAPLUS

CN Isoxazolo[5,4-c]pyridin-3(2H)-one, 4,5,6,7-tetrahydro-, monohydrobromide
 (9CI) (CA INDEX NAME)



● HBr

IT 64603-91-4P
 RL: SPN (Synthetic preparation); PREP (Preparation)
 (preparation of)
 RN 64603-91-4 CAPLUS
 CN Isoxazolo[5,4-c]pyridin-3(2H)-one, 4,5,6,7-tetrahydro- (CA INDEX NAME)



=> FIL STNGUIDE
 COST IN U.S. DOLLARS

| SINCE FILE | TOTAL |
|------------|---------|
| ENTRY | SESSION |
| 74.41 | 249.18 |

FULL ESTIMATED COST

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)

| SINCE FILE | TOTAL |
|------------|---------|
| ENTRY | SESSION |
| -10.14 | -10.14 |

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 AND TECHNOLOGY CORPORATION, AND FACHINFORMATIONSZENTRUM KARLSRUHE

FILE CONTAINS CURRENT INFORMATION.
 LAST RELOADED: May 4, 2007 (20070504/UP).

=> s 13 and leav?

COMBINATION OF STRUCTURE AND TEXT TERMS NOT VALID

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=> s 13 and leav?

COMBINATION OF STRUCTURE AND TEXT TERMS NOT VALID

The query entered contains both search terms created by structure-building or screen commands and text search terms. L#s created via the STRUCTURE or SCREEN commands must be searched in the structures files separately from text terms or profiles. The L# answer sets from structure searches can be used in crossover searches and can be combined with text terms.

=> file caplus

COST IN U.S. DOLLARS

| SINCE FILE | TOTAL |
|------------|---------|
| ENTRY | SESSION |

| | | |
|--|------------------|---------------|
| FULL ESTIMATED COST | 0.48 | 249.66 |
| DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS) | SINCE FILE ENTRY | TOTAL SESSION |
| CA SUBSCRIBER PRICE | 0.00 | -10.14 |

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FILE COVERS 1907 - 9 May 2007 VOL 146 ISS 20
 FILE LAST UPDATED: 8 May 2007 (20070508/ED)

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=> s 13 and leav?
 277799 LEAV?
 L5 0 L3 AND LEAV?

=> s 13
 481 L2
 4400083 PREP/RL
 L6 13 L2/PREP
 (L2 (L) PREP/RL)

=> s 16 and leav?
 277799 LEAV?
 L7 0 L6 AND LEAV?

=> s 16 and react?
 4932193 REACT?
 L8 8 L6 AND REACT?

=> d ibib abs hitstr tot

L8 ANSWER 1 OF 8 CAPLUS COPYRIGHT 2007 ACS on STN
 ACCESSION NUMBER: 2006:1009629 CAPLUS
 DOCUMENT NUMBER: 145:383399
 TITLE: Gaboxadol forms, compositions thereof, methods for preparation and uses for treating sleep disorders
 INVENTOR(S): Almarsson, Orn; Hickey, Magali Bourghol; Peterson, Matthew
 PATENT ASSIGNEE(S): Transform Pharmaceuticals, Inc., USA
 SOURCE: PCT Int. Appl., 56pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------|----------|-----------------|----------|
| WO 2006102093 | A1 | 20060928 | WO 2006-US9737 | 20060317 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |

PRIORITY APPLN. INFO.:

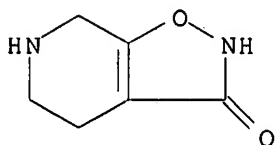
US 2005-663423P P 20050318

AB The invention provides novel gaboxadol forms and methods for making and using the same. These forms include salts, hydrates, solvates, and polymorphs of gaboxadol with improved aqueous solubility when compared to known gaboxadol forms. The invention also provides novel compounds comprising these novel soluble forms and a suitable carrier. The invention also provides related methods of treatment. Compounds and methods of the invention of the invention have a number of uses, including the treatment or prevention of sleep disorders.

IT 815574-58-4P, Gaboxadol monohydrate 910641-51-9P
 RL: PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (gaboxadol forms, compounds thereof, methods for preparation and uses for treating sleep disorders)

RN 815574-58-4 CAPLUS

CN Isoxazolo[5,4-c]pyridin-3(2H)-one, 4,5,6,7-tetrahydro-, monohydrate (9CI) (CA INDEX NAME)



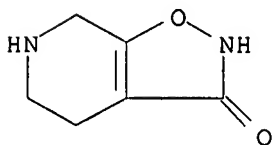
● H₂O

RN 910641-51-9 CAPLUS

CN Isoxazolo[5,4-c]pyridin-3(2H)-one, 4,5,6,7-tetrahydro-, (2Z)-2-butenedioate (9CI) (CA INDEX NAME)

CM 1

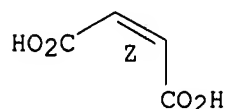
CRN 64603-91-4
 CMF C6 H8 N2 O2



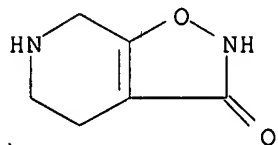
CM 2

CRN 110-16-7
CMF C4 H4 O4

Double bond geometry as shown.



IT 64603-91-4P, Gaboxadol
RL: RCT (Reactant); SPN (Synthetic preparation); PREP
(Preparation); RACT (Reactant or reagent)
(gaboxadol forms, compns. thereof, methods for preparation and uses for
treating sleep disorders)
RN 64603-91-4 CAPLUS
CN Isoxazolo[5,4-c]pyridin-3(2H)-one, 4,5,6,7-tetrahydro- (CA INDEX NAME)



REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

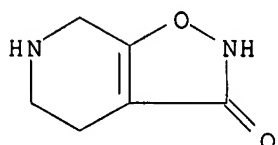
L8 ANSWER 2 OF 8 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2006:795633 CAPLUS
DOCUMENT NUMBER: 145:217970
TITLE: Polymorphic forms of a GABA agonist
INVENTOR(S): Kumke, Daniel J.; Murry, Jerry A.; Simmons, Bryon L.;
Xu, Feng
PATENT ASSIGNEE(S): Merck & Co., Inc., USA
SOURCE: PCT Int. Appl., 12pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---------------|--|----------|-----------------|----------|
| WO 2006083682 | A2 | 20060810 | WO 2006-US2809 | 20060126 |
| WO 2006083682 | A3 | 20070405 | | |
| W: | AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | |
| RW: | AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AP, EA, EP, OA | | | |

PRIORITY APPLN. INFO.: US 2005-648151P P 20050128
AB The present invention is directed to novel polymorphic forms of
4,5,6,7-tetrahydroisoxazolo[5,4-c]pyridin-3-ol hydrate (gaboxadol
monohydrate). The invention is further concerned with pharmaceutical

comps. containing the polymorphic forms as an active ingredient, methods for treatment of disorders susceptible to amelioration by GABAA receptor agonism with the polymorphic forms, and processes for the preparation of the polymorphic forms. Gaboxadol-HCl was dissolved in water-isopropanol and was treated with 1 equiv of 5N NaOH. The solution was stirred and the slurry was aged for hours at ambient temperature. The resulting white solid was filtered and air dried to give the gaboxadol monohydrate form III.

IT 815574-58-4P, Gaboxadol monohydrate
 RL: PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (polymorphic forms of GABA agonist)
 RN 815574-58-4 CAPLUS
 CN Isoxazolo[5,4-c]pyridin-3(2H)-one, 4,5,6,7-tetrahydro-, monohydrate (9CI)
 (CA INDEX NAME)



● H₂O

L8 ANSWER 3 OF 8 CAPLUS COPYRIGHT 2007 ACS on STN
 ACCESSION NUMBER: 2005:238996 CAPLUS
 DOCUMENT NUMBER: 142:316828
 TITLE: Method for the manufacture of THIP
 INVENTOR(S): Petersen, Hans; Bech Sommer, Michael; Dancer, Robert
 PATENT ASSIGNEE(S): H. Lundbeck A/S, Den.
 SOURCE: PCT Int. Appl., 34 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------|----------|------------------|----------|
| WO 2005023820 | A1 | 20050317 | WO 2004-DK579 | 20040901 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | | |
| RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| AU 2004270323 | A1 | 20050317 | AU 2004-270323 | 20040901 |
| CA 2537840 | A1 | 20050317 | CA 2004-2537840 | 20040901 |
| EP 1664060 | A1 | 20060607 | EP 2004-762799 | 20040901 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, HR | | | | |
| CN 1845928 | A | 20061011 | CN 2004-80025424 | 20040901 |
| BR 2004013741 | A | 20061024 | BR 2004-13741 | 20040901 |
| JP 2007504179 | T | 20070301 | JP 2006-525046 | 20040901 |
| NO 2006001424 | A | 20060329 | NO 2006-1424 | 20060329 |

PRIORITY APPLN. INFO.:

DK 2003-1277

A 20030905

US 2003-500422P

P 20030905

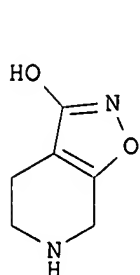
WO 2004-DK579

W 20040901

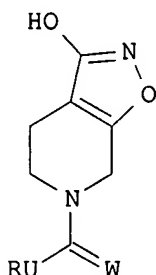
OTHER SOURCE(S):

CASREACT 142:316828; MARPAT 142:316828

GI



I



II

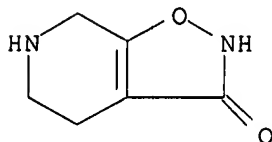
AB The present invention relates to a new method of preparing gaboxadol (THIP; I), which is useful for treating sleep disorders (no data). In particular a method of preparing THIP comprising reacting a compound II [R = alkyl, cycloalkyl, aryl, etc.; U = N, CR1 (R1 = H, R); W = O, S, NR4 (R4 = H, R)] or a salt thereof with an acid, typically a mineral acid, to obtain THIP as an acid addition salt. The present invention also relates to several intermediates. E.g., a multi-step synthesis of I.HBr, starting from Me 3-hydroxyisonicotinate, was given.

IT 65202-63-3P

RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)
(method for the manufacture of THIP)

RN 65202-63-3 CAPLUS

CN Isoxazolo[5,4-c]pyridin-3(2H)-one, 4,5,6,7-tetrahydro-, monohydrobromide (9CI) (CA INDEX NAME)



● HBr

REFERENCE COUNT:

3

THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 4 OF 8 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1984:465548 CAPLUS

DOCUMENT NUMBER: 101:65548

TITLE: Analgesic GABA agonists. Synthesis and structure-activity studies on analogs and derivatives of muscimol and THIP

AUTHOR(S): Haefliger, Walter; Revesz, Laszlo; Maurer, Richard; Roemer, Dietmar; Buescher, Heinz Hermann

CORPORATE SOURCE: Sandoz Ltd., Basel, CH-4002, Switz.

SOURCE: European Journal of Medicinal Chemistry (1984), 19(2), 149-56

CODEN: EJMCA5; ISSN: 0009-4374

DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 101:65548

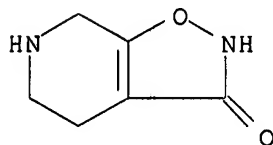
AB A series of analogs. and derivs. (prodrugs) of muscimol and THIP were prepared and their GABA receptor affinity, analgesic, and GABAergic properties examined. Some compds. designed as prodrugs exhibited high GABA receptor affinity indicating that nonzwitterionic mols. interact with GABA receptors. Analgesic and GABAergic activities of muscimol prodrugs were pronounced but weaker than muscimol itself. A ring opened THIP derivative was inactive whereas its carbamate derivative showed analgesic and GABAergic activity. A benzophenone-imine derivative showed strong GABA binding but no analgesic activity. Carbamate type THIP prodrugs were also active in analgesic and anticonvulsive tests but weaker than THIP itself. Ester- and alkanoyloxymethyl prodrugs were only active in the hot plate test. When the inactive 7-methyl-THIP was converted to a potential prodrug it produced high GABA-mimetic activity in both anticonvulsant and analgesic tests. In all cases, sedation was inseparable from analgesia.

IT 64603-91-4DP, derivs.

RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation and GABA agonist activity of, mol. structure in relation to)

RN 64603-91-4 CAPLUS

CN Isoxazolo[5,4-c]pyridin-3(2H)-one, 4,5,6,7-tetrahydro- (CA INDEX NAME)



L8 ANSWER 5 OF 8 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1982:562964 CAPLUS

DOCUMENT NUMBER: 97:162964

TITLE: Isoxazolo[5,4-c]pyridines which are GABA-agonists

INVENTOR(S): Krogsgaard-Larsen, Povl

PATENT ASSIGNEE(S): Lundbeck, H., og Co. A/S, Den.

SOURCE: Can., 29 pp. Division of Can. Appl. No. 305,798.

CODEN: CAXXA4

DOCUMENT TYPE: Patent

LANGUAGE: English

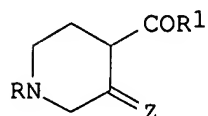
FAMILY ACC. NUM. COUNT: 3

PATENT INFORMATION:

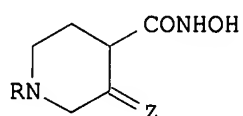
| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------------------|------|----------|-----------------|-------------|
| CA 1125288 | A2 | 19820608 | CA 1981-377128 | 19810507 |
| CA 1107736 | A1 | 19810825 | CA 1978-305798 | 19780620 |
| US 4301287 | A | 19811117 | US 1979-104080 | 19791217 |
| PRIORITY APPLN. INFO.: | | | GB 1977-25740 | A 19770620 |
| | | | CA 1978-305798 | A3 19780620 |
| | | | US 1978-917118 | A3 19780619 |

OTHER SOURCE(S): MARPAT 97:162964

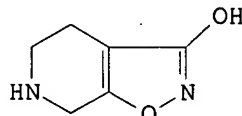
GI



I



II



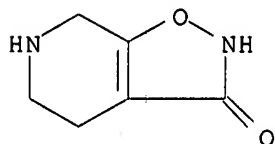
III

AB Piperidinecarboxylic acid compds. I (R = Ac, carbalkoxy, carbophenoxy, CPh3, CHO; Z = ketalized O; R1 = halo, OH, alkoxy) reacted with HONH2 to yield hydroxamic acids II. Isoxazolo[5,4-c]pyridine derivative III, which is an agonist of H2N(CH2)3CO2H, was prepared from II. I (R = CO2Me, R1 = OEt, Z = OCH2CH2O) reacted with HONH2 to give II (R = CO2Me, Z = OCH2CH2O), and the latter was treated with HCl and then with HBr-HOAc to give III.HBr.

IT 64603-91-4P 65202-63-3P
 RL: SPN (Synthetic preparation); PREP (Preparation)
 (preparation and use of, as gamma-aminobutyric acid agonist)

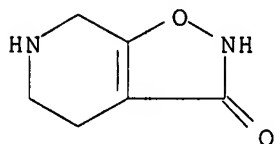
RN 64603-91-4 CAPLUS

CN Isoxazolo[5,4-c]pyridin-3(2H)-one, 4,5,6,7-tetrahydro- (CA INDEX NAME)



RN 65202-63-3 CAPLUS

CN Isoxazolo[5,4-c]pyridin-3(2H)-one, 4,5,6,7-tetrahydro-, monohydrobromide (9CI) (CA INDEX NAME)



● HBr

L8 ANSWER 6 OF 8 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1982:527546 CAPLUS

DOCUMENT NUMBER: 97:127546

TITLE: Deuterium labeling of the GABA agonists THIP, piperidine-4-sulfonic acid, and the GABA uptake inhibitor THPO

AUTHOR(S): Krogsgaard-Larsen, Povl; Johansen, Joergen Stage; Falch, Erik

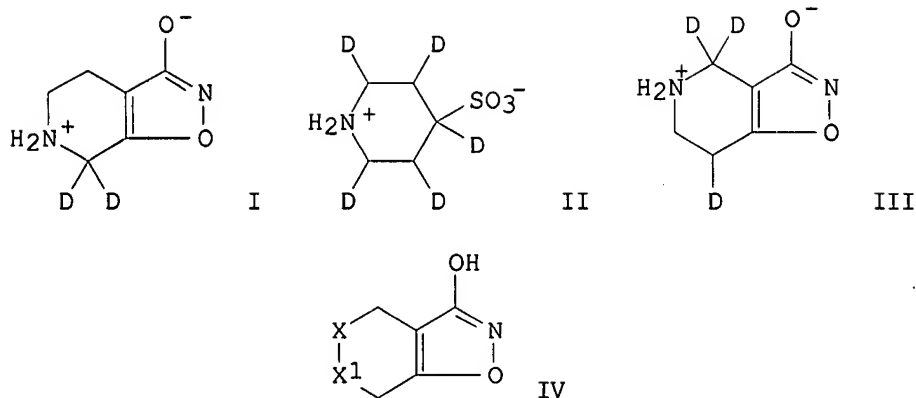
CORPORATE SOURCE: Dep. Chem. BC, R. Dan. Sch. Pharm., Copenhagen, DK-2100, Den.

SOURCE: Journal of Labelled Compounds and Radiopharmaceuticals (1982), 19(5), 689-702
 CODEN: JLCRD4; ISSN: 0362-4803

DOCUMENT TYPE: Journal

LANGUAGE: English

GI

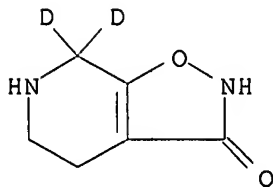


AB The D-labeled title compds. (I, II , and III, resp.) were prepared I and III were prepared from IV (X = CH₂, X1 = NCO₂Me; X = NCO₂Me, X1 = CH₂), resp., by sequential methylation, N-decarboxylation, nitrosation, H-D exchange reaction with D₂O (acid- and base-catalyzed, resp.), denitrosation, and demethylation. Pt-catalyzed deuteration of pyridine-4-sulfonic acid in D₂O gave II.

IT 82988-63-4P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

RN 82988-63-4 CAPLUS

CN Isoxazolo[5,4-c]pyridin-3(2H)-one-7-d, 4,5,6,7-tetrahydro-7-d- (9CI) (CA INDEX NAME)



L8 ANSWER 7 OF 8 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1979:439458 CAPLUS

DOCUMENT NUMBER: 91:39458

TITLE: Methyl tetrahydrohydroxy isoxazolopyridine carboxylate

INVENTOR(S): Krogsgaard-Larsen, Povl

PATENT ASSIGNEE(S): Den.

SOURCE: Jpn. Kokai Tokkyo Koho, 13 pp.
CODEN: JKXXAF

DOCUMENT TYPE: Patent

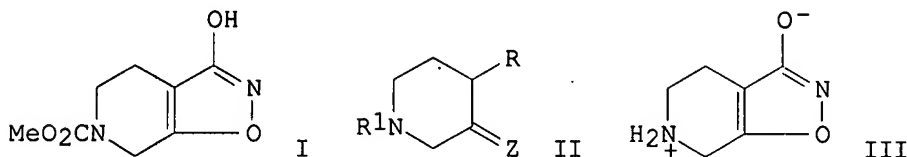
LANGUAGE: Japanese

FAMILY ACC. NUM. COUNT: 3

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|-------------|------|----------|-----------------|----------|
| JP 54036290 | A | 19790316 | JP 1978-74800 | 19780620 |
| DK 7802702 | A | 19781221 | DK 1978-2702 | 19780615 |
| DK 7802703 | A | 19781221 | DK 1978-2703 | 19780615 |
| FI 7801954 | A | 19781221 | FI 1978-1954 | 19780619 |
| FI 64376 | B | 19830729 | | |
| FI 64376 | C | 19831110 | | |
| FI 7801955 | A | 19781221 | FI 1978-1955 | 19780619 |
| NO 7802127 | A | 19781221 | NO 1978-2127 | 19780619 |

| | | | | |
|-----------------------------------|----|----------|-----------------|-------------|
| NO 152049 | B | 19850415 | | |
| NO 152449 | C | 19850724 | | |
| NO 7802128 | A | 19781221 | NO 1978-2128 | 19780619 |
| EP 167 | A1 | 19790110 | EP 1978-100190 | 19780619 |
| R: BE, CH, DE, FR, GB, LU, NL, SE | | | | |
| EP 338 | A2 | 19790124 | EP 1978-100191 | 19780619 |
| EP 338 | A3 | 19790627 | | |
| EP 338 | B1 | 19811125 | | |
| R: BE, CH, DE, FR, GB, LU, NL, SE | | | | |
| ES 470912 | A1 | 19790201 | ES 1978-470912 | 19780619 |
| ES 470913 | A1 | 19790201 | ES 1978-470913 | 19780619 |
| ZA 7803492 | A | 19790627 | ZA 1978-3492 | 19780619 |
| ZA 7803493 | A | 19790627 | ZA 1978-3493 | 19780619 |
| AU 7837244 | A | 19800103 | AU 1978-37244 | 19780619 |
| US 4278676 | A | 19810714 | US 1978-917118 | 19780619 |
| AU 7837298 | A | 19800103 | AU 1978-37298 | 19780620 |
| AU 521040 | B2 | 19820311 | | |
| AT 7804486 | A | 19820215 | AT 1978-4486 | 19780620 |
| AT 368505 | B | 19821025 | | |
| NO 7902839 | A | 19781221 | NO 1979-2839 | 19790903 |
| US 4301287 | A | 19811117 | US 1979-104080 | 19791217 |
| EP 27279 | A1 | 19810422 | EP 1980-106497 | 19801023 |
| R: BE, CH, DE, FR, GB, LU, NL, SE | | | | |
| EP 28017 | A1 | 19810506 | EP 1980-106498 | 19801023 |
| R: BE, CH, DE, FR, GB, LU, NL, SE | | | | |
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| | | | US 1978-917118 | A3 19780619 |
| OTHER SOURCE(S): | | | MARPAT 91:39458 | |
| GI | | | | |

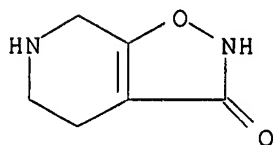


AB The title compound (I) was prepared Thus, (methoxycarbonyl)piperidinone II (R = CO₂Et, R₁ = CO₂Me, Z = O) [obtained by hydrogenating II (R = CO₂Et, R₁ = CH₂Ph, Z = O) over Pd-C; and reacting the product with ClCO₂Me] was ketalized with HOCH₂CH₂OH to give the ethylene acetal II (R = CO₂Et, R₁ = CO₂Me, Z = OCH₂CH₂O), which was treated with H₂NOH.HCl to give II (R = CONHOH, R₁ = CO₂Me, Z = OCH₂CH₂O), whose cyclization in H₂SO₄ gave the hydroxyisoxazolo[5,4-c]pyridinecarboxylate. Decarboxylation of I followed by treatment with HBr and then H₂O-Et₃N-EtOH gave zwitterion III. III was a mild tranquilizer in mice.

IT 64603-91-4P
 RL: SPN (Synthetic preparation); PREP (Preparation)
 (preparation and tranquilizing activity of)

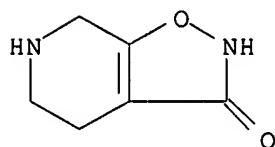
RN 64603-91-4 CAPLUS

CN Isoxazolo[5,4-c]pyridin-3(2H)-one, 4,5,6,7-tetrahydro- (CA INDEX NAME)



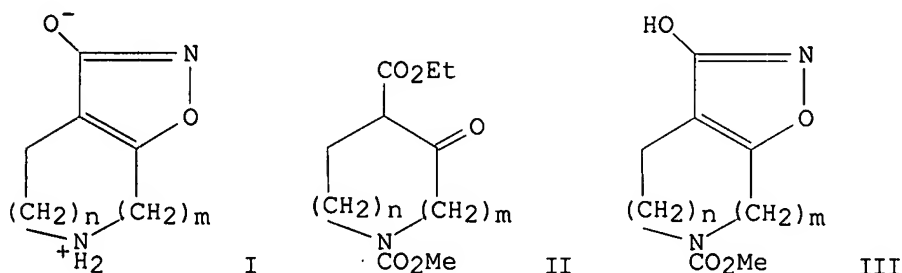
IT 65202-63-3P
 RL: SPN (Synthetic preparation); PREP (Preparation)

(preparation of)
 RN 65202-63-3 CAPLUS
 CN Isoxazolo[5,4-c]pyridin-3(2H)-one, 4,5,6,7-tetrahydro-, monohydrobromide
 (9CI) (CA INDEX NAME)



● HBr

L8 ANSWER 8 OF 8 CAPLUS COPYRIGHT 2007 ACS on STN
 ACCESSION NUMBER: 1978:37672 CAPLUS
 DOCUMENT NUMBER: 88:37672
 TITLE: Muscimol analogs. II. Synthesis of some bicyclic 3-isoxazolol zwitterions
 AUTHOR(S): Krogsgaard-Larsen, Povl
 CORPORATE SOURCE: Dep. Chem. BC, R. Dan. Sch. Pharm., Copenhagen, Den.
 SOURCE: Acta Chemica Scandinavica, Series B: Organic Chemistry and Biochemistry (1977), B31(7), 584-8
 CODEN: ACBOCV; ISSN: 0302-4369
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 OTHER SOURCE(S): CASREACT 88:37672
 GI



AB The 3-isoxazolol zwitterions 4,5,6,7-tetrahydroisoxazolo[5,4-c]pyridin-3-ol, (I, n = 1, m = 1), 5,6,7,8-tetrahydro-4H-isoxazolo[5,4-c]azepin-3-ol (I, n = 2, m = 1), and 5,6,7,8-tetrahydro-4H-isoxazolo[4,5-c]azepin-3-ol (I, n = 0, m = 3) were prepared. The starting materials were the cyclic β -oxoesters II. The ethylene acetals of II were treated with HONH₂ followed by deacetalization and cyclization of the intermediate β -oxohydroxamic acid ethylene acetals to give the resp. 3-isoxazolol derivs. III, which were transformed into the zwitterions I. The pK_a values of I were determined.

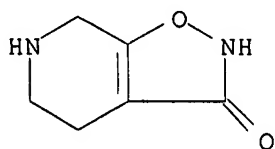
IT 65202-63-3P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation and reaction with triethylamine, zwitterions from)

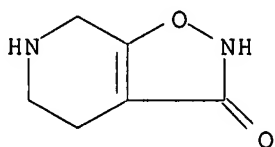
RN 65202-63-3 CAPLUS

CN Isoxazolo[5,4-c]pyridin-3(2H)-one, 4,5,6,7-tetrahydro-, monohydrobromide
 (9CI) (CA INDEX NAME)



● HBr

IT 64603-91-4P
 RL: SPN (Synthetic preparation); PREP (Preparation)
 (preparation of)
 RN 64603-91-4 CAPLUS
 CN Isoxazolo[5,4-c]pyridin-3(2H)-one, 4,5,6,7-tetrahydro- (CA INDEX NAME)



=> FIL STNGUIDE
 COST IN U.S. DOLLARS

| SINCE FILE ENTRY | TOTAL SESSION |
|------------------|---------------|
| 51.14 | 300.80 |

FULL ESTIMATED COST

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)

| SINCE FILE ENTRY | TOTAL SESSION |
|------------------|---------------|
| -6.24 | -16.38 |

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 AND TECHNOLOGY CORPORATION, AND FACHINFORMATIONSZENTRUM KARLSRUHE

FILE CONTAINS CURRENT INFORMATION.
 LAST RELOADED: May 4, 2007 (20070504/UP).

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FILE 'REGISTRY' ENTERED AT 12:38:04 ON 09 MAY 2007

L1 STRUCTURE UPLOADED
 L2 36 S L1 FULL

FILE 'CAPLUS' ENTERED AT 12:41:50 ON 09 MAY 2007

L3 13 S L2/PREP FULL
 L4 0 S L3 AND NUCLEO?

FILE 'STNGUIDE' ENTERED AT 12:44:01 ON 09 MAY 2007

FILE 'CAPLUS' ENTERED AT 12:48:41 ON 09 MAY 2007

L5 0 S L3 AND LEAV?
 L6 13 S L3
 L7 0 S L6 AND LEAV?
 L8 8 S L6 AND REACT?

FILE 'STNGUIDE' ENTERED AT 12:49:42 ON 09 MAY 2007

=> log y

COST IN U.S. DOLLARS

SINCE FILE

TOTAL

ENTRY

SESSION

FULL ESTIMATED COST

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DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)

SINCE FILE

TOTAL

ENTRY

SESSION

CA SUBSCRIBER PRICE

0.00

-16.38

STN INTERNATIONAL LOGOFF AT 12:50:42 ON 09 MAY 2007

Connecting via Winsock to STN

L. 16

Welcome to STN International! Enter x:x

LOGINID:SSPTANXR1625

PASSWORD:

TERMINAL (ENTER 1, 2, 3, OR ?):2

* * * * * Welcome to STN International * * * * *

NEWS 1 Web Page for STN Seminar Schedule - N. America
NEWS 2 JAN 08 CHEMLIST enhanced with New Zealand Inventory of Chemicals
NEWS 3 JAN 16 CA/CAPplus Company Name Thesaurus enhanced and reloaded
NEWS 4 JAN 16 IPC version 2007.01 thesaurus available on STN
NEWS 5 JAN 16 WPIDS/WPINDEX/WPIX enhanced with IPC 8 reclassification data
NEWS 6 JAN 22 CA/CAPplus updated with revised CAS roles
NEWS 7 JAN 22 CA/CAPplus enhanced with patent applications from India
NEWS 8 JAN 29 PHAR reloaded with new search and display fields
NEWS 9 JAN 29 CAS Registry Number crossover limit increased to 300,000 in multiple databases
NEWS 10 FEB 15 PATDPASPC enhanced with Drug Approval numbers
NEWS 11 FEB 15 RUSSIAPAT enhanced with pre-1994 records
NEWS 12 FEB 23 KOREAPAT enhanced with IPC 8 features and functionality
NEWS 13 FEB 26 MEDLINE reloaded with enhancements
NEWS 14 FEB 26 EMBASE enhanced with Clinical Trial Number field
NEWS 15 FEB 26 TOXCENTER enhanced with reloaded MEDLINE
NEWS 16 FEB 26 IFICDB/IFIPAT/IFIUDB reloaded with enhancements
NEWS 17 FEB 26 CAS Registry Number crossover limit increased from 10,000 to 300,000 in multiple databases
NEWS 18 MAR 15 WPIDS/WPIX enhanced with new FRAGHITSTR display format
NEWS 19 MAR 16 CASREACT coverage extended
NEWS 20 MAR 20 MARPAT now updated daily
NEWS 21 MAR 22 LWPI reloaded
NEWS 22 MAR 30 RDISCLOSURE reloaded with enhancements
NEWS 23 APR 02 JICST-EPLUS removed from database clusters and STN
NEWS 24 APR 30 GENBANK reloaded and enhanced with Genome Project ID field
NEWS 25 APR 30 CHEMCATS enhanced with 1.2 million new records
NEWS 26 APR 30 CA/CAPplus enhanced with 1870-1889 U.S. patent records
NEWS 27 APR 30 INPADOC replaced by INPADOCDB on STN
NEWS 28 MAY 01 New CAS web site launched
NEWS 29 MAY 08 CA/CAPplus Indian patent publication number format defined

NEWS EXPRESS NOVEMBER 10 CURRENT WINDOWS VERSION IS V8.01c, CURRENT MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP), AND CURRENT DISCOVER FILE IS DATED 25 SEPTEMBER 2006.

NEWS HOURS STN Operating Hours Plus Help Desk Availability
NEWS LOGIN Welcome Banner and News Items
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Enter NEWS followed by the item number or name to see news on that specific topic.

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FILE 'HOME' ENTERED AT 08:57:09 ON 09 MAY 2007

=> FILE CASREACT

COST IN U.S. DOLLARS

SINCE FILE

TOTAL

ENTRY

SESSION

FULL ESTIMATED COST

0.21

0.21

FILE 'CASREACT' ENTERED AT 08:57:21 ON 09 MAY 2007

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FILE CONTENT:1840 - 5 May 2007 VOL 146 ISS 20

New CAS Information Use Policies, enter HELP USAGETERMS for details.

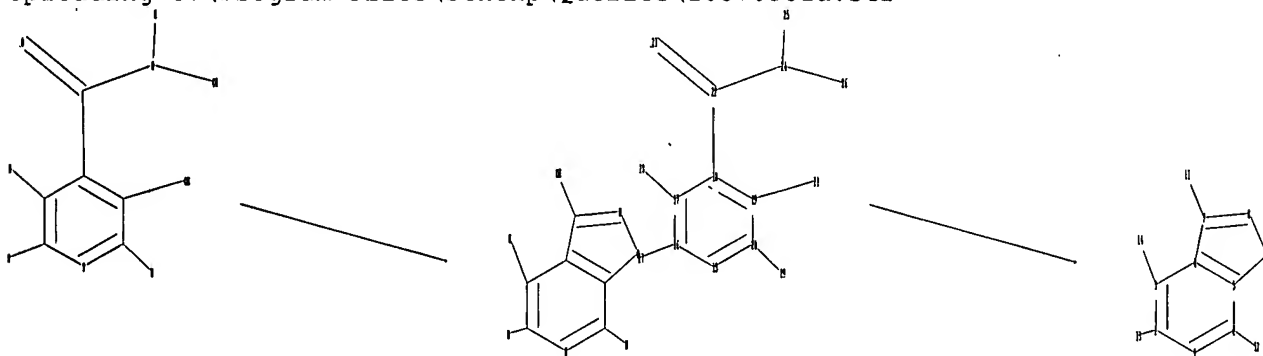
*
* CASREACT now has more than 12 million reactions *
*

Some CASREACT records are derived from the ZIC/VINITI database (1974-1999) provided by InfoChem, INPI data prior to 1986, and Biotransformations database compiled under the direction of Professor Dr. Klaus Kieslich.

This file contains CAS Registry Numbers for easy and accurate substance identification.

=>

Uploading C:\Program Files\Stnexp\Queries\10570551a.str



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ring nodes :

1 2 3 4 5 6 7 8 9 15 16 17 18 19 20

chain bonds :

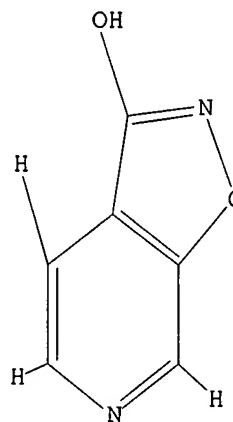
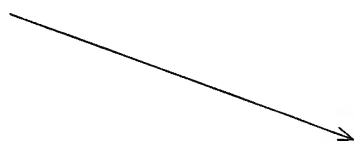
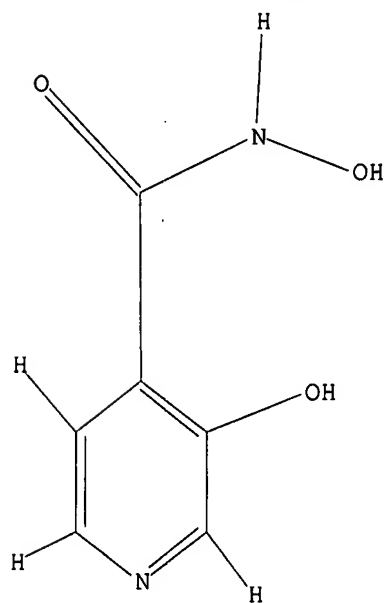
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24-26

ring bonds :
 1-2 1-6 2-3 3-4 4-5 4-7 5-6 5-9 7-8 8-9 15-16 15-20 16-17 17-18 18-19
 19-20
 exact/norm bonds :
 7-8 7-11 19-21 22-23 22-24 24-26
 exact bonds :
 2-13 3-14 4-7 5-9 6-12 8-9 16-27 17-28 18-22 20-29 24-25
 normalized bonds :
 1-2 1-6 2-3 3-4 4-5 5-6 15-16 15-20 16-17 17-18 18-19 19-20
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 containing 1 : 15 :

Match level :
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 12:CLASS 13:CLASS 14:CLASS 15:Atom 16:Atom 17:Atom 18:Atom 19:Atom 20:Atom
 21:CLASS 22:CLASS 23:CLASS 24:CLASS 25:CLASS 26:CLASS 27:CLASS 28:CLASS
 29:CLASS
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 containing 1
 fragments assigned reactant/reagent role:
 containing 15

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 L1 STR



Structure attributes must be viewed using STN Express query preparation.

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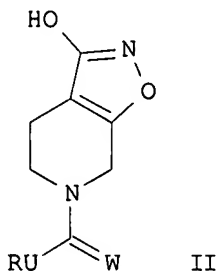
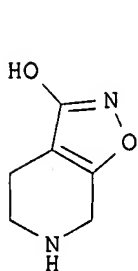
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SEARCH TIME: 00.00.01

L2 1 SEA SSS FUL L1 (2 REACTIONS)

=> d ibib abs fhit

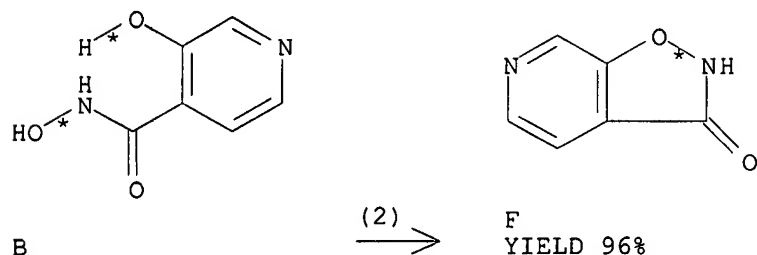
L2 ANSWER 1 OF 1 CASREACT COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 142:316828 CASREACT
TITLE: Method for the manufacture of THIP
INVENTOR(S): Petersen, Hans; Bech Sommer, Michael; Dancer, Robert
PATENT ASSIGNEE(S): H. Lundbeck A/S, Den.
SOURCE: PCT Int. Appl., 34 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------------------|--|----------|------------------|----------|
| WO 2005023820 | A1 | 20050317 | WO 2004-DK579 | 20040901 |
| W: | AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | |
| RW: | BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | |
| AU 2004270323 | A1 | 20050317 | AU 2004-270323 | 20040901 |
| CA 2537840 | A1 | 20050317 | CA 2004-2537840 | 20040901 |
| EP 1664060 | A1 | 20060607 | EP 2004-762799 | 20040901 |
| R: | AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, HR | | | |
| CN 1845928 | A | 20061011 | CN 2004-80025424 | 20040901 |
| BR 2004013741 | A | 20061024 | BR 2004-13741 | 20040901 |
| JP 2007504179 | T | 20070301 | JP 2006-525046 | 20040901 |
| NO 2006001424 | A | 20060329 | NO 2006-1424 | 20060329 |
| PRIORITY APPLN. INFO.: | | | DK 2003-1277 | 20030905 |
| | | | US 2003-500422P | 20030905 |
| | | | WO 2004-DK579 | 20040901 |
| OTHER SOURCE(S): | MARPAT 142:316828 | | | |
| GI | | | | |



AB The present invention relates to a new method of preparing gaboxadol (THIP; I), which is useful for treating sleep disorders (no data). In particular a method of preparing THIP comprising reacting a compound II [R = alkyl, cycloalkyl, aryl, etc.; U = N, CR1 (R1 = H, R); W = O, S, NR4 (R4 = H, R)] or a salt thereof with an acid, typically a mineral acid, to obtain THIP as an acid addition salt. The present invention also relates to several intermediates. E.g., a multi-step synthesis of I.HBr, starting from Me 3-hydroxyisonicotinate, was given.

RX(2) OF 15 ...B ==> F...



RX(2) RCT B 89640-77-7
RGT G 530-62-1 Diimidazolyl ketone
PRO F 847996-42-3
SOL 68-12-2 DMF
CON SUBSTAGE(1) room temperature
SUBSTAGE(2) overnight, room temperature

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> d his

(FILE 'HOME' ENTERED AT 08:57:09 ON 09 MAY 2007)

FILE 'CASREACT' ENTERED AT 08:57:21 ON 09 MAY 2007

L1 STRUCTURE UPLOADED
L2 1 S L1 FULL

=> log y

| | | |
|--|------------------|---------------|
| COST IN U.S. DOLLARS | SINCE FILE ENTRY | TOTAL SESSION |
| FULL ESTIMATED COST | 118.47 | 118.68 |
| DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS) | SINCE FILE ENTRY | TOTAL SESSION |
| CA SUBSCRIBER PRICE | -0.73 | -0.73 |

STN INTERNATIONAL LOGOFF AT 08:58:14 ON 09 MAY 2007

claim 1

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Welcome to STN International! Enter x:x

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PASSWORD:

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* * * * * Welcome to STN International * * * * *

| | | | |
|--------------|----|--------|--|
| NEWS | 1 | | Web Page for STN Seminar Schedule - N. America |
| NEWS | 2 | JAN 08 | CHEMLIST enhanced with New Zealand Inventory of Chemicals |
| NEWS | 3 | JAN 16 | CA/CAPplus Company Name Thesaurus enhanced and reloaded |
| NEWS | 4 | JAN 16 | IPC version 2007.01 thesaurus available on STN |
| NEWS | 5 | JAN 16 | WPIDS/WPINDEX/WPIX enhanced with IPC 8 reclassification data |
| NEWS | 6 | JAN 22 | CA/CAPplus updated with revised CAS roles |
| NEWS | 7 | JAN 22 | CA/CAPplus enhanced with patent applications from India |
| NEWS | 8 | JAN 29 | PHAR reloaded with new search and display fields |
| NEWS | 9 | JAN 29 | CAS Registry Number crossover limit increased to 300,000 in multiple databases |
| NEWS | 10 | FEB 15 | PATDPASPC enhanced with Drug Approval numbers |
| NEWS | 11 | FEB 15 | RUSSIAPAT enhanced with pre-1994 records |
| NEWS | 12 | FEB 23 | KOREAPAT enhanced with IPC 8 features and functionality |
| NEWS | 13 | FEB 26 | MEDLINE reloaded with enhancements |
| NEWS | 14 | FEB 26 | EMBASE enhanced with Clinical Trial Number field |
| NEWS | 15 | FEB 26 | TOXCENTER enhanced with reloaded MEDLINE |
| NEWS | 16 | FEB 26 | IFICDB/IFIPAT/IFIUDB reloaded with enhancements |
| NEWS | 17 | FEB 26 | CAS Registry Number crossover limit increased from 10,000 to 300,000 in multiple databases |
| NEWS | 18 | MAR 15 | WPIDS/WPIX enhanced with new FRAGHITSTR display format |
| NEWS | 19 | MAR 16 | CASREACT coverage extended |
| NEWS | 20 | MAR 20 | MARPAT now updated daily |
| NEWS | 21 | MAR 22 | LWPI reloaded |
| NEWS | 22 | MAR 30 | RDISCLOSURE reloaded with enhancements |
| NEWS | 23 | APR 02 | JICST-EPLUS removed from database clusters and STN |
| NEWS | 24 | APR 30 | GENBANK reloaded and enhanced with Genome Project ID field |
| NEWS | 25 | APR 30 | CHEMCATS enhanced with 1.2 million new records |
| NEWS | 26 | APR 30 | CA/CAPplus enhanced with 1870-1889 U.S. patent records |
| NEWS | 27 | APR 30 | INPADOC replaced by INPADOCDB on STN |
| NEWS | 28 | MAY 01 | New CAS web site launched |
| NEWS | 29 | MAY 08 | CA/CAPplus Indian patent publication number format defined |
| NEWS EXPRESS | | | NOVEMBER 10 CURRENT WINDOWS VERSION IS V8.01c, CURRENT MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP), AND CURRENT DISCOVER FILE IS DATED 25 SEPTEMBER 2006. |
| NEWS HOURS | | | STN Operating Hours Plus Help Desk Availability |
| NEWS LOGIN | | | Welcome Banner and News Items |
| NEWS IPC8 | | | For general information regarding STN implementation of IPC 8 |

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FILE 'HOME' ENTERED AT 08:49:51 ON 09 MAY 2007

=> file casreact

COST IN U.S. DOLLARS

SINCE FILE

TOTAL

ENTRY

SESSION

FULL ESTIMATED COST

0.21

0.21

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FILE CONTENT:1840 - 5 May 2007 VOL 146 ISS 20

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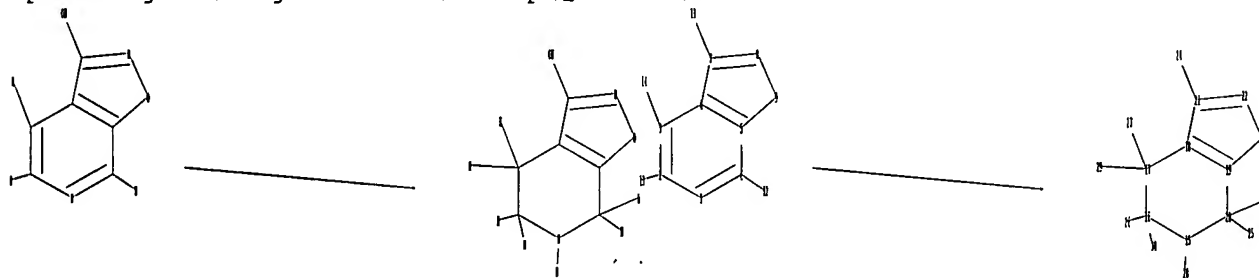
*
* CASREACT now has more than 12 million reactions *
*

Some CASREACT records are derived from the ZIC/VINITI database (1974-1999) provided by InfoChem, INPI data prior to 1986, and Biotransformations database compiled under the direction of Professor Dr. Klaus Kieslich.

This file contains CAS Registry Numbers for easy and accurate substance identification.

=>

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chain nodes :

11 12 13 14 24 25 26 27 28 29 30 31

ring nodes :

1 2 3 4 5 6 7 8 9 15 16 17 18 19 20 21 22 23

chain bonds :

2-13 3-14 6-12 7-11 15-28 16-26 16-30 17-27 17-29 20-25 20-31 21-24

ring bonds :

1-2 1-6 2-3 3-4 4-5 4-7 5-6 5-9 7-8 8-9 15-16 15-20 16-17 17-18 18-19
18-21 19-20 19-23 21-22 22-23

exact/norm bonds :

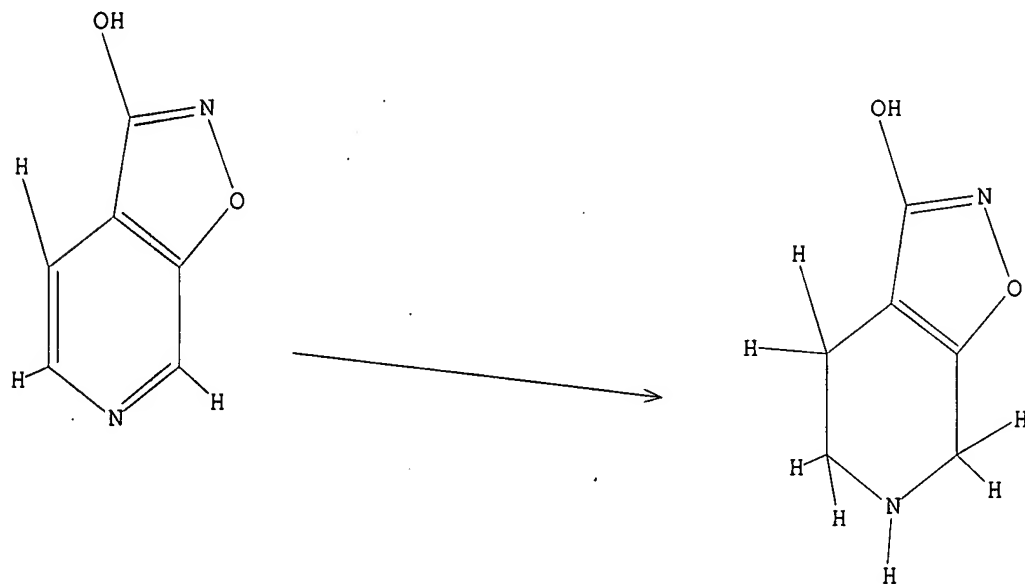
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22-23

exact bonds :
 2-13 3-14 4-7 5-9 6-12 8-9 15-28 16-26 16-30 17-27 17-29 20-25 20-31
 normalized bonds :
 1-2 1-6 2-3 3-4 4-5 5-6
 isolated ring systems :
 containing 1 :

Match level :
 1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 11:CLASS
 12:CLASS 13:CLASS 14:CLASS 15:Atom 16:Atom 17:Atom 18:Atom 19:Atom 20:Atom
 21:Atom 22:Atom 23:Atom 24:CLASS 25:CLASS 26:CLASS 27:CLASS 28:CLASS
 29:CLASS 30:CLASS 31:CLASS
 fragments assigned product role:
 containing 15
 fragments assigned reactant/reagent role:
 containing 1

L1 STRUCTURE UPLOADED

=> d l1
 L1 HAS NO ANSWERS
 L1 STR



Structure attributes must be viewed using STN Express query preparation.

=> s l1 full
 FULL SEARCH INITIATED 08:51:09 FILE 'CASREACT'
 SCREENING COMPLETE - 3 REACTIONS TO VERIFY FROM 1 DOCUMENTS
 100.0% DONE 3 VERIFIED 2 HIT RXNS 1 DOCS
 SEARCH TIME: 00.00.01

L2 1 SEA SSS FUL L1 (2 REACTIONS)

=> d ibib abs fhitr tot
 'FHITSTR' IS NOT A VALID FORMAT FOR FILE 'CASREACT'

The following are valid formats:

ABS ----- GI and AB
ALL ----- BIB, AB, IND, RE, Single-step Reactions
APPS ----- AI, PRAI
BIB ----- AN, plus Bibliographic Data
CAN ----- List of CA abstract numbers without answer numbers
CBIB ----- AN, plus Compressed Bibliographic Data
DALL ----- ALL, delimited (end of each field identified)
IABS ----- ABS, indented with text labels
IALL ----- ALL, indented with text labels
IBIB ----- BIB, indented with text labels
IND ----- Indexing data
IPC ----- International Patent Classifications
ISTD ----- STD, indented with text labels
OBIB ----- AN, plus Bibliographic Data (original)
OIBIB ----- OBIB, indented with text labels

SBIB ----- BIB, no citations
SIBIB ----- IBIB, no citations

MAX ----- Same as ALL
PATS ----- PI, SO
SCAN ----- TI and FCRD (random display, no answer number. SCAN
must be entered on the same line as DISPLAY, e.g.,
D SCAN.)
SSRX ----- Single-Step Reactions (Map, Diagram, and Summary for
all single-step reactions)
STD ----- BIB, IPC, and NCL

CRD ----- Compact Display of All Hit Reactions
CRDREF ----- Compact Reaction Display and SO, PY for Reference
FHIT ----- Reaction Map, Diagram, and Summary for first
hit reaction
FHITCBIB --- FHIT, AN plus CBIB
FCRD ----- First hit in Compact Reaction Display (CRD) format
FCRDREF ---- First hit in Compact Reaction Display (CRD) format with
CA reference information (SO, PY). (Default)
FPATH ----- PATH, plus Reaction Summary for the "long path"
FSPATH ----- SPATH, plus Reaction Summary for the "short path"
HIT ----- Reaction Map, Reaction Diagram, and Reaction
Summary for all hit reactions and fields containing
hit terms
OCC ----- All hit fields and the number of occurrences of the
hit terms in each field. Includes total number of
HIT, PATH, SPATH reactions. Labels reactions that have
incomplete verifications.
PATH ----- Reaction Map and Reaction Diagram for the "long
path". Displays all hit reactions, except those
whose steps are totally included within another hit
reaction which is displayed
RX ----- Hit Reactions (Map, Diagram, Summary for all hit reactions)
RXG ----- Hit Reaction Graphics (Map and Diagram for all hit reactions)
RXL ----- Hit Reaction Long (Map, Diagram, Summary for all hit reactions)
RXS ----- Hit Reaction Summaries (Map and Summary for all hit reactions)
SPATH ----- Reaction Map and Reaction Diagram for the "short
path". Displays all single step reactions which
contain a hit substance. Also displays those
multistep reactions that have a hit substance in both
the first and last steps of the reaction, except for
those hit reactions whose steps are totally included
within another hit reaction which is displayed

To display a particular field or fields, enter the display field
codes. For a list of the display field codes, enter HELP DFIELDS

at an arrow prompt (=>). Examples of combinations include: D TI;
D BIB RX; D TI, AU, FCRD. The information is displayed in the same order
as the specification. All of the formats, except CRD, CRDREF, FHIT, PATH,
FPATH, SPATH, FSPATH, FCRD, FCRDREF, HIT, RX, RXG, RXS, SCAN, and OCC, may
be used with the DISPLAY command to display the record for a specified
Accession Number.

ENTER DISPLAY FORMAT (FCRDREF):cbib

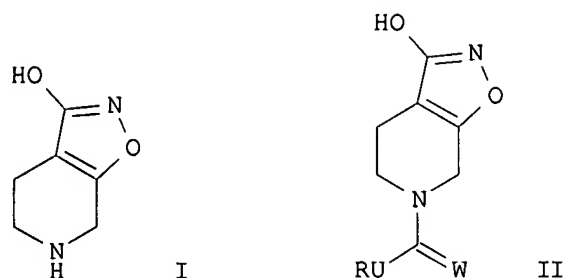
L2 ANSWER 1 OF 1 CASREACT COPYRIGHT 2007 ACS on STN
142:316828 Method for the manufacture of THIP. Petersen, Hans; Bech Sommer,
Michael; Dancer, Robert (H. Lundbeck A/S, Den.). PCT Int. Appl. WO
2005023820 A1 20050317, 34 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT,
AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK,
DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS,
JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN,
MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG,
SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM,
ZW; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA,
GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR.
(English). CODEN: PIXXD2. APPLICATION: WO 2004-DK579 20040901.
PRIORITY: DK 2003-1277 20030905; US 2003-2003/PV500422 20030905.

=> d ibib abs fhit

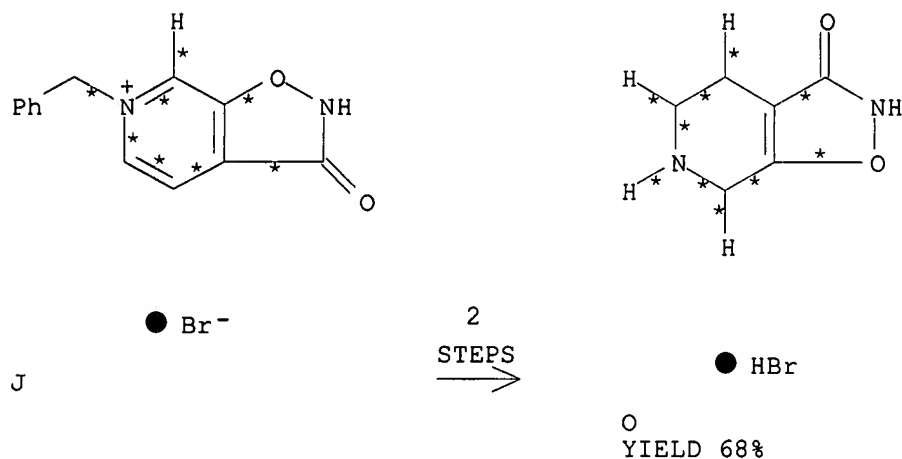
L2 ANSWER 1 OF 1 CASREACT COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 142:316828 CASREACT
TITLE: Method for the manufacture of THIP
INVENTOR(S): Petersen, Hans; Bech Sommer, Michael; Dancer, Robert
PATENT ASSIGNEE(S): H. Lundbeck A/S, Den.
SOURCE: PCT Int. Appl., 34 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------------------|------|----------|--|----------|
| WO 2005023820 | A1 | 20050317 | WO 2004-DK579 | 20040901 |
| W: | | | AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | |
| RW: | | | BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | |
| AU 2004270323 | A1 | 20050317 | AU 2004-270323 | 20040901 |
| CA 2537840 | A1 | 20050317 | CA 2004-2537840 | 20040901 |
| EP 1664060 | A1 | 20060607 | EP 2004-762799 | 20040901 |
| R: | | | AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, HR | |
| CN 1845928 | A | 20061011 | CN 2004-80025424 | 20040901 |
| BR 2004013741 | A | 20061024 | BR 2004-13741 | 20040901 |
| JP 2007504179 | T | 20070301 | JP 2006-525046 | 20040901 |
| NO 2006001424 | A | 20060329 | NO 2006-1424 | 20060329 |
| PRIORITY APPLN. INFO.: | | | DK 2003-1277 | 20030905 |
| | | | US 2003-500422P | 20030905 |

MARPAT 142:316828



AB The present invention relates to a new method of preparing gaboxadol (THIP; I), which is useful for treating sleep disorders (no data). In particular a method of preparing THIP comprising reacting a compound II [R = alkyl, cycloalkyl, aryl, etc.; U = N, CR¹ (R¹ = H, R); W = O, S, NR⁴ (R⁴ = H, R)] or a salt thereof with an acid, typically a mineral acid, to obtain THIP as an acid addition salt. The present invention also relates to several intermediates. E.g., a multi-step synthesis of I.HBr, starting from Me 3-hydroxyisonicotinate, was given.

$$\begin{array}{l} \text{RX(9) OF 15 COMPOSED OF RX(4), RX(5)} \\ \text{RX(9) } J \implies 0 \end{array}$$


RX (4) RCT J 847996-43-4
 RGT M 16940-66-2 NaBH4
 PRO L 847996-44-5
 SOL 7732-18-5 Water, 64-17-5 EtOH
 CON SUBSTAGE(1) <35 deg C
 SUBSTAGE(2) 24 hours
 NTE caution reagent foams on addition

RX (5) RCT L 847996-44-5

STAGE (1)

RGT P 7087-68-5 EtN(Pr-i)2, Q 79-22-1 ClCO2Me

SOL 141-78-6 AcOEt
CON SUBSTAGE(1) room temperature
SUBSTAGE(2) 48 hours, room temperature
SUBSTAGE(3) room temperature -> 0 deg C

STAGE(2)
RGT R 7664-41-7 NH3
SOL 7732-18-5 Water
CON SUBSTAGE(2) 15 minutes

STAGE(3)
RGT S 10035-10-6 HBr
SOL 64-19-7 AcOH
CON SUBSTAGE(2) 6 hours, 40 deg C

PRO O 65202-63-3
REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> d his

(FILE 'HOME' ENTERED AT 08:49:51 ON 09 MAY 2007)

FILE 'CASREACT' ENTERED AT 08:50:30 ON 09 MAY 2007

L1 STRUCTURE UPLOADED
L2 1 S L1 FULL

=> log y

| | | |
|--|------------|---------|
| COST IN U.S. DOLLARS | SINCE FILE | TOTAL |
| | ENTRY | SESSION |
| FULL ESTIMATED COST | 120.95 | 121.16 |
| DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS) | SINCE FILE | TOTAL |
| | ENTRY | SESSION |
| CA SUBSCRIBER PRICE | -0.73 | -0.73 |

STN INTERNATIONAL LOGOFF AT 08:53:01 ON 09 MAY 2007